WASHINGTON NEWS

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GOP COMMITTEE PROPOSES PARTNERSHIP HEALTH PROGRAM

A national Republican committee task force on "Human Rights and Needs" called for a five-point "partnership" health program to be carried out by federal, state, and local governments. At the same time, the committee rejected as "unsound" proposals to extend the social security system to cover health care for the aged.

Recommended goals of the six-member committee of government and private experts included enlarging the capacity of medical schools so that 3,000 more physicians could be graduated each year; providing more hospital and nursing-home beds; and supplementing hospital facilities with clinics, day-care centers, and more visiting nurses to care for patients in their own homes.

Continued federal support for basic medical research "should be accomplished in a manner that will encourage the maximum possible increase in nonfederal support of research and that will not result in too great a diversion into research of doctors required for the urgent needs of teaching and medical practice," the group stated.

The report was one of a series of reports by task forces of the Republican committee on program and progress that has been setting forth party goals and proposals for the federal government's role in all fields.

By 1965, the committee predicted spending 1 billion dollars annually—equally divided between the federal government and nonfederal sources—would be required for medical research.

A five-point "partnership" program was set forth, incl[illegible]ng (1) short-term federal aid for construction of [illegible]al school buildings; (2) changes in the prese[illegible]ospital construction program to encourage renova[illegible] and repair of outmoded hospitals; (3) federal guarantees of mortgages to encourage construction of private nursing homes on a basis assuring high standards of construction and operation; (4) encouragement of construction of diagnostic and outpatient facilities in rural areas and the building of mental health clinics; and (5) federal aid to cities "in more effective planning and coordination of health services."

The committee also recommended vigorous federal support of preventive health programs, and expansion and greater flexibility of voluntary health insurance programs.

"A free people and a free medical profession can achieve these goals with the wise support of government, without bureaucratic restrictions or interference with the physician-patient relationship which has made American health services a model for the free world," the committee said.

As for proposals in Congress to broaden the *social security system to include health care for the* elderly, the committee said "Such a law would represent an irreversible decision to abandon voluntary insurance for the aged in the hospital field and would probably mark the beginning of the end of voluntary insurance for the aged in the health field generally.

"Private insuring organizations and medical associations are in the process of developing medical and health insurance programs which will meet the needs and fit the pocketbooks of people over 65. Ultimately it should be possible for a person to purchase, through payments in advance of retirement, insurance against the concern that postretirement illness might wipe out a lifetime's savings."

Members of the committee are: Bertha S. Adkins, Undersecretary of Health, Education and Welfare; Benjamin S. Adamowski, state's attorney, Cook County, Illinois; Corinne B. Galvin, professor at Ithaca College, New York; Mrs. Oliver R. Rowe, President of Mecklenburg County, North Carolina, Republican Women's Club; George M. Shapiro New York City attorney, and Cecil H. Underwood Governor of West Virginia.

HEALTH MANPOWER REPORT

A Public Health Service report said the number of graduating students at medical schools will have to increase substantially to avoid a decline in the ratio of physicians to the population. Unless there is a step-up in such graduations, the ratio will drop to 126 physicians per 100,000 persons by 1975, compared with the current range of 131 to 135 to 100,000, the report said.

The report, entitled "Health Manpower Source Book, Section 9: Physicians, Dentists and Nurses," also indicated that the ratio of dentists would decline even more sharply.

This year, the 85 medical schools in the United States graduated 6,895 physicians. To maintain the present physician-population ratio, the report declared, U. S. medical schools would need to graduate about 10,360 students by 1975—nearly 3,000 above the 7,410 graduates currently predicted for that year.

The 47 dental schools graduated 3,083 dentists in the academic year 1957-1958. Despite the addition of eight new dental schools since World War II and large increase in the number of graduates, the ratio of dentists to population remains below pre-World War II levels. This decline is expected to continue, PHS said. To regain the current dentist-population ratio, about 2,700 more dental graduates above the number currently predicted will be needed in 1975. This calls for a 75% increase in the number of dental students who, according to present estimates, will be graduates during that year.

According to the report, the ratio of dentists was 62 per 100,000 in 1940, 57 in 1958, and is expected to decline to about 50 per 100,000 by 1975.

There should, however, be an increase in the ratio of professional nurses—from 268 per 100,000 population in 1958 to 284 per 100,000 in 1970, the report indicates. The nurse-population ratio has increased almost fivefold in the United States since 1910.

The report said the current combined ratio of doctors of medicine and osteopathy to population is about 140 per 100,000 persons. This is expected to decline to 133 per 100,000 by 1975.

The District of Columbia was reported to have the highest ratio of physicians to population—302.9 per 100,000. New York led the states with 191.2 physicians per 100,000.

The report is the latest in a series on health manpower, and contains state and regional as well as national data. Listed as Public Health Service publication no. 263, section 9, it may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 50 cents per copy. Single free copies may be obtained from the Division of Public Health Methods, Public Health Service, Washington 25, D. C.

SURGEON GENERAL SUGGESTS INFLUENZA VACCINATION

U. S. Surgeon General Leroy E. Burney recomended that certain groups seriously consider vaccination before the influenza season starts. He listed hese groups as (1) persons for whom the onset of fluenza might represent an added health risk, such those with cardiovascular or pulmonary condions, persons over the age of 55 years with chronic lness of any type, and pregnant women; (2) persons responsible for the care of the sick; (3) persons responsible for providing essential public services; and (4) industries and other commercial enterprises wishing to keep the employee absenteeism rate from rising.

Dr. Burney said no widespread attacks of influenza are presently anticipated but that localized outbreaks of the disease undoubtedly will occur during the next several months, "and vaccination is considered a prudent measure for the groups and individuals named."

He added that the predominant type of influenza this fall and winter probably will be the A-2, or Asian strain, rather than influenza-B which was the major form last year.

CASES OF POLIOMYELITIS DECREASE

The Public Health Service reported that the incidence of poliomyelitis was dropping through the last weeks of September and early October. After an upsurge in early September after a previous decline, the number of cases began falling off again later in the month.

There were 279 cases of paralytic poliomyelitis during the week ended Oct. 3, compared with 304 and a peak 332 in the two previous weeks. For the latest week, small localized concentrations of cases continued, scattered about the country. New outbreaks were recognized in North Carolina and Tennessee. Little activity was reported in areas of previous epidemics and no new epidemics were reported.

Through the week ending Oct. 3, a total of 4,013 paralytic cases were listed for the year, in contrast to 1,931 during the same 1958 span and 7,886 in 1955, the first year the Salk vaccine became generally available.

PHS said the vaccine supply situation had improved, "and the acute shortages experienced by some U. S. communities during late July and August apparently no longer exist."

In a previous report, PHS said the increase in cases of poliomyelitis this year did not reflect on the efficacy of the Salk vaccine, since most of the cases were in persons who had not received the required vaccine dosage.

PERSONNEL

Dr. Aims C. McGuinness, special assistant for health and medical affairs to the Secretary of Health, Education and Welfare, resigned after three years in the post. In accepting the resignation, President Eisenhower said McGuinness had "helped significantly in the development of an effective health program for the American people."

Dr. Robert L. Bennett, Warm Springs, Ga., was named to the national advisory council on vocational rehabilitation of the Department of Health, Education and Welfare to succeed Dr. Frank H. Krusen, who resigned to become special assistant for health and medical affairs to Miss Mary E. Switzer, director of the office of vocational rehabilitation.

The exceptional service award of the Veterans Administration was presented to Dr. Ma[illegible] M. Cummings for his work as director of medical research for the VA. Dr. Cummings left the VA to become chairman of the department of microbiology at the Oklahoma University School of Medicine.

Dr. Clifton K. Himmelsbach was appointed associate director of the clinical center of the National Institutes of Health, succeeding the late Dr. Kenneth W. Chapman. Dr. Himmelsbach has been with the U. S. Public Health Service since 1931. He is an expert in the pharmacology of drug addiction.

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The girl was 2 years old when her mother went to the hospital to deliver her third child, a boy. She was kept by her aunt while her mother was in the hospital. "While at her aunt's she began to spend time rocking back and forth on the floor. She became afraid of cars and of being left alone. Feeding and sleeping problems also started. When it was brought to our pediatrician's attention he said to bring her home immediately, which we did. Following this, she had a bladder infection which was treated with shots for over a year. Mary became intensely afraid of the doctor during this time and began to be afraid of any man, including her daddy. She would go screaming through the house, shutting all doors as she went, until she was in the farthest closet. There she would be found, sitting and rocking on the floor.

"Our pediatrician refused to recognize these symptoms at this time, saying that I was an overanxious mother and Mary was a spoiled child. Her fears continued to grow [and] her cries [became] sharper and her screaming more intense until August, when the doctor suggested putting her in nursery school to break up what he called 'the strong mother-daughter tie.' This we did in a nursery school one block away. She seemed to enjoy the first half-hour or so, but when I left to go home she started screaming hysterically. I took her home in a state of shock, and every time I moved her in my arms she clung and started to scream. The mucus ran from her mouth and she had a lost, wild look. Mary regressed very rapidly from this point, almost into infancy. She slept in a fetal position and the sitting and screaming became much worse, with poor appetite, little sleep, and rocking during the night.

"I was frantic and, receiving no help from my pediatrician, contacted another friend who sent me to her doctor. He referred us to another pediatrician who sedated her and sent her to a psychologist. He tested Mary and diagnosed her as [having] 'complete brain damage.' At this point Mary's fear of the car, noises, and vibrations was so great that when we took her to the psychologist she was stiff in my arms, almost unconscious. Many varied diagnoses and treatment approaches followed. It wasn't until she entered the hospital at the age of 7 years that we finally realized she was suffering from childhood schizophrenia."

Just as cancer must be treated early to secure a reasonable chance of success, so childhood schizophrenics should have treatment as early as possible. Certainly part of the reason for the present poor prognosis in this condition is due to the delay in onset of therapy.

Methods of Study

The children at Camarillo State Hospital Children's Unit were studied intensively by us. For a complete description as well as a detailed discussion of diagnostic criteria, readers are referred to another publication.[1]

Diagnosis was established by observation in eight areas: appearance, speech, motility and posture, play patterns, interpersonal responses, thought content, psychometrics, and clinical history. Admission to the hospital and diagnoses were made by other psychiatrists, and in all the children included in the study the opinion was unanimous among at least three psychiatrists (and concurred in by us) that the child should be classed as a "childhood schizophrenic." The group studied consisted of 34 schizophrenic children, of whom 30 were hospitalized at the time. All had developed clinical schizophrenia before the age of 5 years.

In an effort to determine what the initial signs and symptoms are, a detailed questionnaire was filled out by the parents of these children. As a control, parents of 14 hospitalized and 5 nonhospitalized children with behavior disorders filled out the same questionnaire. The hospitalized children with behavior disorders were living with the schizophrenic children. The answers to most of the 70 items on the questionnaire showed no significant difference between the two groups, as would be expected. There were, however, 25 significant items, and from them a picture of a young schizophrenic child can be assembled.

Results

Results can be grouped under three headings—decreased socialization, unusual play patterns, and neurophysiological disturbances. These classifications are arbitrary and there is considerable overlapping, but the dichotomy does have some value.

Evidence of Decreased Socialization.—Indications of decreased socialization are found in the following eight questions, which reflected eight significant differences between the schizophrenic and the nonschizophrenic child. All the questions have been slightly rephrased and were originally in a form which gave the parent the chance of answering on a continuum varying from "very frequently" to "seldom." 1. The schizophrenic child played games like "patty-cake," "bye-bye," and "so-big" less frequently than the nonschizophrenic child. 2. Interest in surroundings in the early months of life was much less in most of the schizophrenic children. 3. The schizophrenic child was more of a behavior problem after the arrival of a new baby in the family than was the nonschizophrenic child. 4. In keeping with the above, the ability of most of the schizophrenic children to share with a brother or sister was very much less than that of the nonschizophrenic children. 5. Toilet-training the schizophrenic child was more of a problem. 6. Nighttime bladder training was also a great problem in the schizophrenic child, much more so than in the nonschizophrenic. 7. Parents of schizophrenic children felt that the home situation had improved to a great extent since the hospitalization of the child, while parents of the nonschizophrenic children thought it had improved only slightly. 8. Masturbation was often uninhibited and usually much more frequent among the schizophrenic as compared to the nonschizophrenic children.

The above findings were in keeping with the general impression that schizophrenic children very early show signs of decreased interest in their surroundings and in other children and people. They were less impressed by standards of social values and therefore had much less motivation to train themselves in bowel and bladder control. Many of the children in the study had not obtained this control when they entered the hospital at the age of 6 or 7 years. The greater improvement in the home situation after their hospitalization showed how much more disturbing the schizophrenic child was considered to be by the parents.

Evidence of Unusual Play Patterns.—There were eight questions concerning which there was a statistical difference between the schizophrenic and behavior-problem children. 1. Interest in music was more likely to be great in the schizophrenic than in the nonschizophrenic child. 2. The schizophrenic children were often preoccupied in their early years with stacking blocks or placing items next to one another for long periods of time, sometimes for hours. This was not found to any great extent in the nonschizophrenic children. 3. There was a great deal of difficulty in changing the schizophrenic child's interest once he had established a play pattern, whereas there was only a moderate amount of difficulty in distracting the nonschizophrenic child. 4. Schizophrenic children often had a great interest in spinning toys, such as tops and wheels, and this was infrequent among the nonschizophrenic children. 5. Interest in round objects was especially great among the schizophrenic children. 6. Compared to the nonschizophrenic children, the schizophrenic children were often interested in climbing up on tables and jumping off, as well as in jumping off other objects onto the floor. 7. Interest in boats or water play was especially great among the schizophrenic children; this seemed to be one of their chief diversions. 8. Pica (placing nonedible objects in the mouth) was observed frequently in the schizophrenic children but was relatively rare among the other children.

The finding that there was great difficulty in changing the play patterns of schizophrenic children is consistent with general clinical experience; parents often complained that they could not change them from one activity to another. This interest in sameness is quite in contrast to that of the organically disturbed child, who is more apt to have a short attention span and to flit from one activity to another.

Evidence of Neurophysiological Disturbance.—Seven questions, answers to which were significant among the parents of schizophrenic children, seem to be more closely related to neurophysiological disturbance than some of the previously mentioned items. 1. Among the schizophrenic children the sleeping pattern was a great problem. 2. Some of the children would cling to the parent with a tenacious grip. This occurred in a significant number of the schizophrenic children and was rarely reported in the nonschizophrenic children. 3. Many schizophrenic children would frequently slap their heads or otherwise hit themselves, at the same time being fairly oblivious to any ensuing pain.[2] 4. An unusual symptom seen almost exclusively among schizophrenic children was sensitivity to sounds and loud noises which would not bother the average child or adult.[3] 5. Another unusual symptom seen in these schizophrenic children was persistent toe-walking, a subject commented on previously by us.[4] 6. The schizophrenic child showed a much greater interest in moving objects, such as swings, merry-go-rounds, cars, or airplanes, than did the nonschizophrenic child. 7. A symptom seen almost exclusively among school-age schizophrenic children was the tendency to whirl themselves about in circles spontaneously.

This pattern of disturbances, seemingly based on neurophysiological changes but with no evidence of neurological damage, is seen consistently among schizophrenic children. The clinging behavior is comparable to the "symbiosis" of Mahler.[5] Occasionally the whirling is seen in children with brain damage and is therefore not diagnostic of childhood schizophrenia.

Comment

It has been the feeling of several investigators, including Bender[6] and Fish,[7] that childhood schizophrenics often have neurophysiological manifestations of their condition which can be noted clinically at an early age. Fish has reported her preliminary work in which these manifestations were used for the successful diagnosis of the condition within the first 6 months of life, with confirmation by the later development of the child.

It is difficult to say what the causes of the neurophysiological changes are, but they lead to interesting speculations. Certainly there is evidence that some schizophrenics have difficulty in conceiving the position of their bodies in space, as was pointed out by Schilder many years ago.[8] It appears likely that this disturbance is responsible for the toe-walking, the preoccupation with spinning toys, and the attraction for jumping from heights. Some of these symptoms may result directly from this confusion about space, and others perhaps represent a way in which the children attempt to solve their confusion through repeated testing.

The repetitive play pattern and the difficulty in getting them to change their play from one activity to another may be another example of the children's attempt to reassure themselves about their own bodies and environments. By repeating over and over again the play pattern that they are familiar with they try to avoid the confusion resulting from new experiences. With this disturbance in the concept of their own bodies it it also possible to understand why they would cling to the few objects they are sure of, including mother.

One of the most prominent neurophysiological disturbances is in the area of vestibular function, as we pointed out in a previous study of these same children.[1] Many of the schizophrenic children showed minimal or no reaction to caloric vestibular stimulation. Perhaps, because of resultant confusion about spatial orientation, they are not able to progress in learning about their bodies and themselves in relation to the outside world and continue to have a disorganized concept of what this relationship is. It may be connected with what Bender[9] calls "maturational lag." She pointed out that these children showed normal progression in some areas but retarded development in other physiological areas. Vestibular function may be a prominent area in which maturation is delayed ("lags").

As time goes on, and the children continue to be at a disadvantage, they adopt many symptoms of more immature behavior which help to reassure them but make them more and more odd in comparison to their peers. Thus, initial dysfunction may be compounded by attempts to compensate. The ultimate condition of childhood schizophrenia is a conglomeration of disturbed physiology and disturbed psychology, combined with compensatory reactions. Withdrawal from reality, often the most obvious symptom, is really more a compensation than an original symptom.

As was evidenced by the case of Mary, psychological and standard neurological examinations are generally not helpful with these children, and the primary diagnosis must be made by careful developmental history and clinical examination. Although there may be a disorder of the neurochemical or neurophysiological substrates in the brain in this condition, it is not of the order that will become manifest on general clinical examination of reflexes and of motor skill. The child with definite evidence of localized brain damage is not similar to the childhood schizophrenic and his problems are different from those of the schizophrenic child. Any brain changes in childhood schizophrenia are undoubtedly subtle and widespread, with no evidence of localized destruction of brain tissue. A possible site of the origin of the most significant neurophysiological changes is the reticular core, since this area of the brain influences both upstream and downstream conduction and in general is the only area which has an influence on every other area; disease or abnormality here could account for the widespread neurophysiological changes noticed in childhood schizophrenia. Definition of the extent of the disorder in this area and the specific nature of it will have to wait for more refined research techniques and more knowledge of how brain function is integrated.

Implications for the Family Physician

Early diagnosis in childhood behavior disorders and early referral to appropriate treatment facilities are vital if any progress is to be made in treating childhood schizophrenia.

In making referrals to any psychiatric facility it is most important to adopt a noncritical attitude in dealing with the parents. An excess of sympathy for the child can do much to place the blame on the parents and may indeed block any further investigations of the problem. If questioned about the etiology of childhood schizophrenia by a parent, one must state that medicine does not yet know the answer. It can certainly be said that no dynamic factor can of itself produce schizophrenia in a child and that the child must have an X factor, or constitutional predisposition, which of itself or in combination with stress produces the syndrome.

We have seen many children who have had an "autistic" response in the 1st year of life, in the presence of both adequate and inadequate parents. The behavior of these parents was often rejecting when the children were first seen in the clinic at the age of 5 or 6 years, but was this rejection primary or secondary? Peck and co-workers[10] studied the parents of over 200 schizophrenic children and found the one group characteristic to be the reaction to the child's illness. They believed that the parents' problems arose from this reaction. Erickson[11] also noticed the problem within the child and stated that in the cases of infantile schizophrenia which he has seen there is a primary deficiency in "sending" power within the child.

Many of our patients appear to have done well until the 3rd year of life and then to have regressed when some incident occurred which would have bothered a normal child only mildly, such as the mother's going to the hospital or the birth of a new sibling. These events are trying times in any young life, but they can be surmounted by the majority of children. Here, too, the problem appeared to be within the child and may indeed be an inability to differentiate himself from his mother.[5]

It is important to emphasize that constitutional factors play a role in childhood schizophrenia; overemphasis on the role of the parents in producing the illness has been partly responsible for the tremendous guilt which is characteristic of these parents and which interferes with therapy. The historical development of methods of treatment in childhood schizophrenia is partly responsible for the guilty reaction of parents. Treatment of neurotic children has been traditionally done in child guidance clinics in the United States and has emphasized the role of the parents (particularly the mother) in producing the emotional pathology. Out of this grew the well-known phrase, "There are no bad children, only bad parents."

When childhood schizophrenia became recognized during the 1940's as an important syndrome, it was thought by many to be just another emotional reaction in childhood and therefore was gathered under the protective wing of the child guidance clinic. It was also assumed that the parents were to blame, and treatment emphasized the role of the mother in producing the condition.

Parents are assailed through the mass culture mediums such as television and national magazines about their role in "causing" emotional problems in children, and they accept their burden of guilt without much question. Little information is available to parents concerning the constitutional factors in childhood schizophrenia, and they are assured by the child guidance authorities that parental rejection is the etiological agent. The resultant guilt often becomes so overwhelming that many are unable to take their hospitalized children out for visits for fear of again "injuring" them.

Questions of adoption concerning infants of schizophrenic mothers are frequently asked of physicians. We have seen at least two cases in which children of schizophrenic mothers were never legally adopted by the new parents because of their fear of schizophrenia. This, of course, is a situation to be avoided. On the other hand, we have also seen many instances in which no mention was made of any possible inherited factor. This approach is equally at fault.[12] Obviously the child deserves a warm, affectionate household, and the adoptive parent should know that he may face a problem in the future.

In the final analysis, it should be stated that we do not have sufficient explanation of the genesis to be sure about the optimal treatment for childhood schizophrenia. Bender's follow-up studies have shown that two-thirds of the children who were childhood schizophrenics were out of hospitals and doing fairly well in their teens and later. We must discover the reason for the differences in the outcome of these patients, many of whom were not treated with psychotherapy. An accepting home and an accepting school situation appear to be important factors in determining a good prognosis. Hospitalization, while often necessary, tends to isolate the child. It is to be hoped that day-care centers will be the ultimate answer to the treatment problem in childhood schizophrenia, at least in many cases. They will only succeed if parents can be helped to accept their role and the child's role in a treatment program of many years' duration.

Summary and Conclusions

Parents of schizophrenic children were questioned about the early symptoms of their children and the results were compared with the responses of the parents of children with behavior disorders. Many areas of significant difference were found. These fell into the broad general categories of decreased socialization, abnormal play patterns, and evidence of neurophysiological disturbance.

There was disorder in many areas, including the sleep pattern. Many of the symptoms showed the concern of the child with the relationship of his body to the external world. Related to this was the tendency to be preoccupied with spinning objects, a lack of interest in other people and other children, and a tendency to withdraw from the external world. Play patterns were repetitive and it was difficult to get the children to change their play, probably on the basis of the function of this symptom as an attempt to reassure the child about his own position in space. Persistent toe-walking and spontaneous whirling were frequently noted.

This study tends to confirm the belief that there is evidence of neurophysiological differences between schizophrenic and nonschizophrenic children. The possible site of dysfunction in this disease is in the brain stem reticular core, but it is emphasized that the changes are subtle and widespread over the entire nervous system. The main method of diagnosis is by developmental history and clinical observation of the neurophysiological status of the patient, with attention to the degree of socialization and the play pattern. This is primarily the responsibility of the physician; results of psychological testing have been disappointing with these children and are almost completely valueless with those under 5 years of age.

One of the problems in the treatment of childhood schizophrenia is the usual delay in diagnosis, which often renders treatment impractical because of the many years the condition has gone unrecognized. With increased awareness by the family physician and pediatrician, it is probable that treatment will be more successful and that many more of these children will become useful citizens.

Dr. Norbert Rieger, Chief of the Children's Unit of Camarillo State Hospital, cooperated in carrying out the research involved in this study.

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ELECTROENCEPHALOGRAPHIC ABNORMALITY IN "UNCOMPLICATED" CHILDHOOD DISEASES

Frederic A. Gibbs, M.D., Erna L. Gibbs, Phyllis R. Carpenter, M.D.
and
Harold W. Spies, M.D., Chicago

Clinically evident encephalitis occurs as a relatively infrequent complication of measles, mumps, chickenpox, rubella (German measles), and scarlet fever. The incidence of these types of encephalitis varies from year to year, from one locality to another, with the age of the patients, and with the different diseases. The reported incidence ranges from one in 428 to one in 1,300.[1] Our previously reported [2] and present observations indicate, however, that children with supposedly uncomplicated measles, mumps, chickenpox, rubella, and scarlet fever often show electroencephalographic evidence of brain involvement. Follow-up studies are needed to assess the long-term effects of such involvement, but the present evidence indicates clearly that the number of cases in which the brain is affected is far greater than the number with clinically obvious encephalitis.

Materials and Method

Electroencephalographic tracings were obtained on [illegible] to the Municipal Contagious Disease Hospital of Chicago from Oct. 15, 1956, to Oct. 15, 1958, with a diagnosis of measles, mumps, chickenpox, rubella, or scarlet fever. The total number of patients was 1,298 and the number in each diagnostic category is shown in the table. Patients were carefully observed in order to detect any symptoms indicative of central nervous system complications. The initial recording was made from one to three days after admission and usually

Electroencephalograms were obtained from 1,298 children who had been admitted to a hospital with diagnoses of measles, mumps, chickenpox, rubella, or scarlet fever. The tracings were studied in relation to clinical evidence of encephalitic processes accompanying these diseases. The body temperature itself was not a factor, and normal EEG's were obtained in a number of patients whose rectal temperatures exceeded 40 C (104 F). Of 717 patients with measles, 37 had clinical evidence of encephalitis and all of the 37 had abnormal EEG's; of the 680 patients with measles without clinical evidence of encephalitis, 344 (51%) had abnormally slow EEG's during the acute or immediate postacute phase of their illness. The probability of brain involvement was greatest at the age of 3 years for measles and chickenpox, and 2 years for mumps. Of the five diseases studied, rubella was the least likely and measles the most likely to be accompanied by clinical or electroencephalographic evidence of encephalitis. In three cases impairment of intellectual ability and general behavior was noted in spite of a return of the EEG to normal. The number of patients in whom the brain is affected by these diseases is far greater than the number with clinically obvious encephalitis.

From the Department of Neurology and Neurological Surgery, University of Illinois, School of Medicine, and the Municipal Hospital for Contagious Diseases.

two to seven days after the onset of symptoms. The usual antipyretic treatment with aspirin and tepid sponges was used to control fever. All patients with scarlet fever received procaine penicillin for 7 to 10 days. Children with other diseases were given antibiotics only if bacterial infections, such as otitis media, sinusitis, or pneumonia, were present.

Electroencephalographic recordings were made on a Grass eight-channel console (model III D) while the patient was awake and, in most cases, also while asleep. Electrodes were applied to the frontal, parietal, temporal, and occipital areas on each side and to the lobes of both ears. Interconnected ear lobes were used as a common reference (monopolar recording). Normal and abnormal electroencephalograms were evaluated according to the standards for age in the "Atlas of Electroencephalography."[3]

Abnormal Electroencephalographic Tracings in Contagious Childhood Diseases

Disease		EEG Abnormal in Acute or Immediate Postacute Phase		Convulsions in Acute Phase		Convulsions in Chronic Phase	
		No.	%	No.	%	No.	%
Measles	680	344	51	49	7		
Measles encephalitis	37	37	100	17	46	6	16
Mumps	110	34	31	2	3		
Mumps encephalitis	16	16	100	6	38	2	12
Chickenpox	237	48	22	8	3		
Chickenpox encephalitis	16	16	100	6	38	1	6
Scarlet fever	156	33	21	1	0.6		
Rubella	45	6	12				
Rubella encephalitis	1	1	100				
Total	1,298						

Patients whose records showed abnormalities were given repeat tests within a week, and then at longer intervals as indicated until the tracing returned to normal or became stabilized.

Patients showing signs or symptoms of encephalitis were followed up with repeated tracings, some for as long as two and one-half years, and will be reported in another communication.

Results

At the beginning of this study we tried to eliminate fever as a factor by recording the electroencephalograms only when the child's rectal temperature was below 101.6 F (38.1 C). The objection could still be raised, however, that the slow activity was the result of either the present mild fever or a residual of high fever. We checked a number of cases and found no correlation between the level of the patient's fever prior to the electroencephalographic study and the presence or absence of slow waves. Some children who had very little fever had extreme slowing, whereas others who had very high fever (sometimes with pneumonia) had no electroencephalographic abnormality. In order to investigate the question further, electroencephalograms were scheduled for 340 consecutive patients without regard to the presence or absence of fever. The rectal temperature of the patient was measured at the time of the electroencephalographic recording. The findings are set forth in figure 1; from this it will be seen that there is no significant relationship in these cases between the degree of electroencephalographic abnormality and the body temperature.

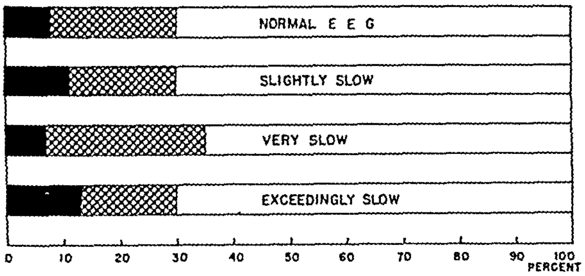

Fig. 1.—Incidence of normal and elevated temperatures in children with normal and abnormal electroencephalograms during and immediately after infectious diseases of childhood. Black portion of column shows percentage of patients with particular type of electroencephalogram, indicated by label of column, who had rectal temperature above 102 F; double crosshatched portion, 100-102 F; white portion, below 100 F. Figure should be read as follows: 8% of children with normal electroencephalogram had greatly elevated temperatures (102-104 F).

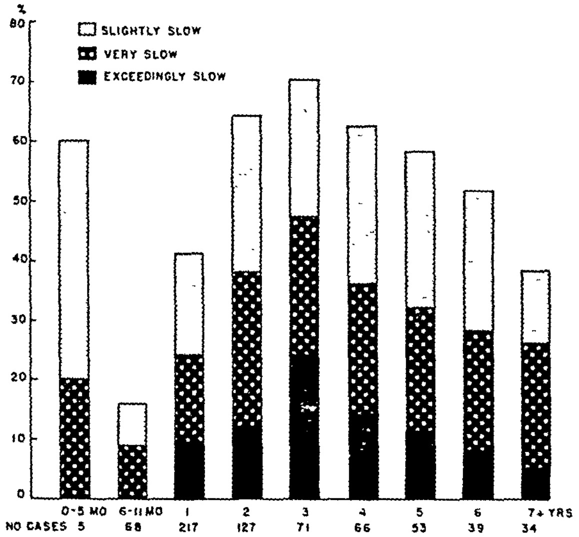

Fig. 2.—Incidence, degree, and age distribution of abnormal electroencephalograms in acute and immediate postacute phase of measles, without clinical evidence of encephalitis (680 cases). Number of cases in first age group is insufficient to make percentage reliable; included merely to show that, although measles in youngest age group is rare, it may produce electroencephalographic abnormality when it occurs.

Measles.—Because of a high incidence of measles in Chicago during the period of our study, we were able to obtain recordings on a large number of patients with this disease. Of the 717 patients studied, 37 had clinically evident encephalitis. All with encephalitis had abnormal electroencephalograms, and 51% of the 680 patients with no clinical evidence of encephalitis had abnormally slow electroencephalograms during the acute or immediate postacute phase of their illness (see table).

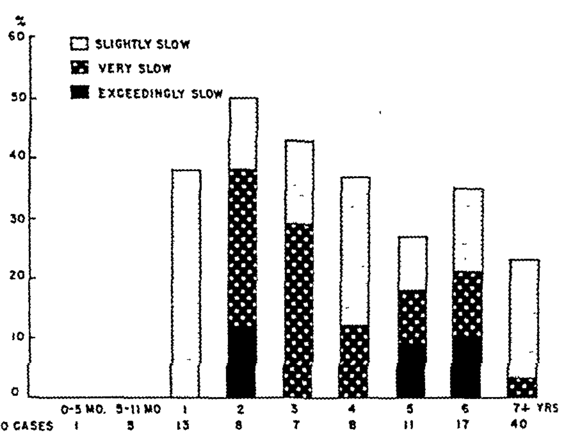

Fig. 3.—Incidence and degree of electroencephalographic abnormality among children of various ages in acute and postacute stage of mumps, without clinical evidence of encephalitis (110 cases).

Figure 2 shows the age distribution and the incidence and degree of electroencephalographic abnormality among children with measles having no clinical evidence of encephalitis. As will be seen from figure 2, it is at 3 years of age that children are maximally susceptible to brain involvement by measles as judged by electroencephalographic abnormality; 72% of children 3 years of age had abnormal electroencephalograms and 25% of children in this age group had electroencephalograms that were extremely abnormal.

Mumps.—Of 126 patients with mumps, 16 had clinically evident encephalitis. All patients with encephalitis and 31% of the 110 patients with no clinical evidence of encephalitis had slow electroencephalograms in the acute and immediate postacute phase (see table).

Figure 3 shows the age distribution and the incidence and degree of electroencephalographic abnormality among children with mumps and without clinical evidence of encephalitis. With this disease the highest incidence of brain involvement, as judged by electroencephalographic abnormality, is at the age of 2 years.

Chickenpox.—Two hundred fifty-three patients with chickenpox were studied. Sixteen of these had clinically evident encephalitis; in all cases their electroencephalograms were abnormal. Of the remaining 237 patients who had no clinical signs of central nervous system involvement, 22% had abnormal electroencephalograms in the acute or immediate postacute phase. The age distribution of these cases and the incidence of abnormality are shown in figure 4. The peak incidence of brain involvement as judged by the electroencephalogram was at 3 years of age.

Rubella.—Because rubella is ordinarily a very mild disease which does not require hospitalization, we had not expected to have an opportunity to study it. However, shortly after the present project got under way, many cases of this disease occurred in several "children's homes" in the Chicago area. The patients were sent to the hospital for isolation and thus became available for our study. Recordings were obtained on 46 of these children. In this group, one child had clinically evident encephalitis and his electroencephalogram was abnormal. Six of the remaining 45 (12%) had abnormal electroencephalograms. The number of cases was too small to provide significant information regarding age distribution, but the incidence and degree of abnormality in the group without clinical evidence of encephalitis are shown in figure 6.

Scarlet Fever.—In addition to the findings among children with viral diseases, interest attaches to changes in patients with scarlet fever. Of 156 children with scarlet fever, none had clinical evidence of encephalitis. Twenty-one per cent had abnormally slow electroencephalograms in the acute or immediate postacute phase of their illness (see table). The age distribution and the incidence and degree of abnormality are shown in figure 5. The highest incidence of abnormality, but also the least severe, occurred at 5 years of age; but there was no definite peak. Children of all ages from 2 to 6 years seem to be equally prone to develop slow activity during scarlet fever.

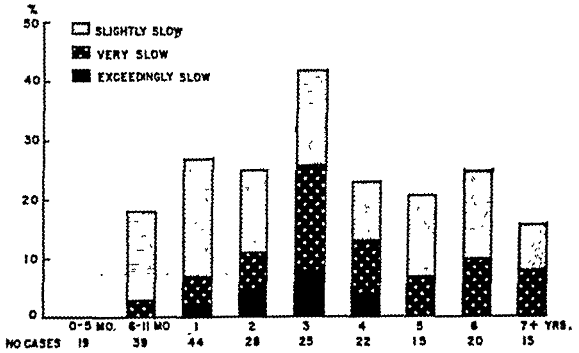

Fig. 4.—Incidence and degree of electroencephalographic abnormality among children of various ages in acute and postacute stage of chickenpox, without clinical evidence of encephalitis (237 cases).

Comment.—Figure 6 is a summary of the foregoing findings. It shows the incidence of various degrees of abnormality in supposedly uncomplicated cases of the common contagious diseases of childhood without regard to age, with measles as the worst offender and rubella as the most innocuous; only in one case where there was clinical evidence of encephalitis did rubella produce extreme abnormality.

Follow-up Studies

As part of our follow-up study on these children we have recorded 904 electroencephalograms at the time of return visits to the hospital. These recordings were all made on children who showed persistent slow activity at the time of their discharge. The study is continuing and it is still too early to make a definitive report of our findings. However, only 1% of those patients who showed electroencephalographic abnormality in the acute or immediate postacute phase continue to show persistent electroencephalographic abnormality for months or years afterward (fig. 7 and 8). In some cases the slow activity is replaced by low-voltage spikes, usually in the occipital area. These may increase in voltage and after an initial period of increase they may subside. We have seen patients in whom the electroencephalogram eventually normalized who did not develop symptoms, even though spikes developed and were present for a period of some months. Two patients whom we followed up closely, because they showed persistent electroencephalographic abnormality and increasing spike activity, developed convulsions (fig. 7).

Comment

High-voltage slow waves in the postacute and chronic stage, which are later mixed with spikes of varying voltage and location, have been described in clinically evident encephalitis occurring as a complication of the common contagious diseases of childhood.[4] Such cases are not without interest, and this part of the over-all problem will be dealt with in later publications. In this report we are concerned with cases of common contagious childhood diseases without clinical evidence of brain disorder.

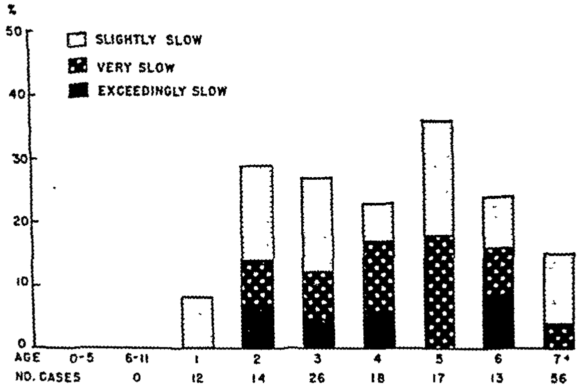

Fig. 5.—Incidence and degree of electroencephalographic abnormality among children of various ages in acute and postacute stages of scarlet fever, without clinical evidence of encephalitis (156 cases).

The results of this study indicate that for every case of evident clinical encephalitis there are hundreds of cases in which the childhood illness is accompanied by electroencephalographic abnormalities. These are not due to fever. The incidence and degree of abnormality vary from one disease to another and from one age to another. The period of maximum vulnerability as indicated by the electroencephalogram is in the 3rd year of life for measles and chickenpox but for mumps it is in the 2nd year. Children of all ages below 7 years seem to be about equally vulnerable to brain involvement by scarlet fever.

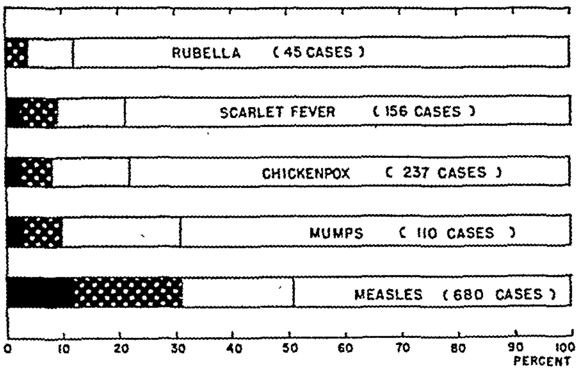

Fig. 6.—Summary of incidence and degree of electroencephalographic abnormality in acute and postacute stage of infectious diseases of childhood, without clinical evidence of encephalitis; black section represents "exceedingly abnormally slow"; black and white "abnormally slow"; and gray "slightly slow."

The question may arise as to whether the transient appearance of slow activity in the electroencephalogram is of any practical importance. The question may also be asked as to whether persistent and increasing abnormality is of real clinical significance. We believe that the answer to both these questions in the light of the total evidence is in the affirmative. How significant it is remains to be determined; it can only be determined by follow-up studies which are reinforced by cross-sectional studies on normal and abnormal persons at various ages. These are under way but, in the meantime, we believe that there is good reason to accept the electroencephalographic abnormalities that appear during the acute and postacute phase of the common diseases of childhood as evidence of a type of disorder which is similar to, but less severe than, the types of cerebral disorder occurring in cases of clinical encephalitis. Since clinical signs and symptoms are less sensitive indicators and are present only in those cases with evidence of severe damage, we believe that the electroencephalograph allows us to detect mild damage.

We have watched the development and evolution of increasing electroencephalographic abnormality after measles in two patients. Both have gone on to have convulsions. One was diagnosed as having "idiopathic epilepsy" by the family physician after his third convulsion. We knew, of course, that this was not a case of "idiopathic epilepsy" but a case of postmeasles epilepsy, because we watched the entire process develop from continuous very slow activity during the acute phase of measles to slow activity mixed with very low-voltage spikes; these gradually changed to high-voltage spikes. We know that this type of electroencephalogram is usually associated with a history of seizures and we had expected seizures to occur.

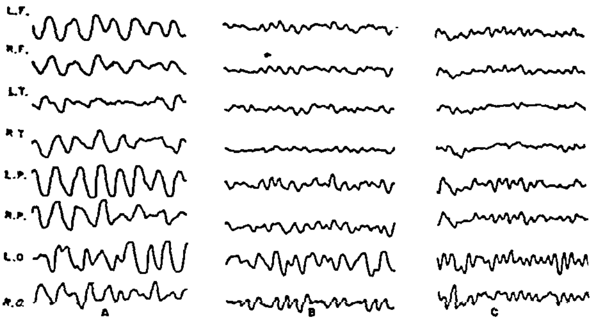

Fig. 7.—Electroencephalographic evidence of subclinical brain disorder produced by measles, with subsequent prompt recovery. *A*, exceedingly abnormal slow electroencephalogram of 5-year-old boy with measles (rectal temperature 99 F); no clinical evidence of brain involvement. *B*, 10 days later, greatly improved; slightly slow activity in all leads and slow wave focus in left occipital area. *C*, three weeks after first recording (shown in *A*), electroencephalogram normal.

What percentage of patients will subsequently develop convulsions or neurological symptoms cannot be estimated from the small number of cases and the short experience that we have had thus far. The present evidence indicates, however, that the common contagious diseases can produce late sequelae in children who show no clinical evidence of brain involvement during the acute or postacute phase of the disease.

Even though a child's electroencephalogram returns to normal, there is the possibility that significant injury has occurred which may cause subsequent emotional instability, psychiatric symptoms, or a reduction of intellectual power. We know that in cases of encephalitis which are followed by severe behavior disturbances or intellectual defects without convulsions, the electroencephalogram commonly normalizes. In hypsarhythmia [5] the electroencephalogram from the 1st to the 3rd year of life is usually extremely abnormal and epileptiform attacks are frequent; in the 3rd year of life seizures often cease and the electroencephalogram commonly normalizes, but the child is usually left with a severe intellectual defect. Postencephalitic paralysis agitans (parkinsonism) and postencephalitic chorea (for example, Sydenham's chorea) are usually associated with normal electroencephalograms, even though during the acute phase of the encephalitis which initiated the cerebral disease process the electroencephalogram was abnormal.

In our follow-up studies we have three cases in which the child's parents and teachers have reported behavior disturbances and decrease in the child's intellectual ability after recovery from measles, in spite of a return of the electroencephalogram to normal. No case of this type has been reported to us from the group of children whose electroencephalograms remained normal throughout their illnesses.

If we are to identify all the disturbances produced by childhood diseases we cannot assume that a return of the electroencephalogram to normal means that the brain has not been injured. Many things can go wrong with the brain and still not show in the electroencephalogram. However, by interpreting both the negative and the positive findings in the light of what we know about the uses and limitations of electroencephalography, we may be able to get clews to some of the factors underlying behavior disorders, intellectual retardation, mental disease, and epilepsy in that great majority of cases where the cause is at present unknown.

Summary and Conclusions

Electroencephalographic tracings obtained from 1,298 patients who had measles, mumps, chickenpox, rubella (German measles), or scarlet fever supposedly uncomplicated by central nervous system involvement, if judged by clinical signs and symptoms, show a high percentage of cases with marked electroencephalographic abnormalities during the acute and postacute periods. The great majority of these cases clear up within 10 days but some do not.

Long-term follow-up of as many of these children as possible is under way to determine the ultimate outcome. Two children whose electroencephalograms did not normalize have developed convulsions. It seems possible that childhood contagious diseases are responsible for more central nervous system disease than is generally supposed.

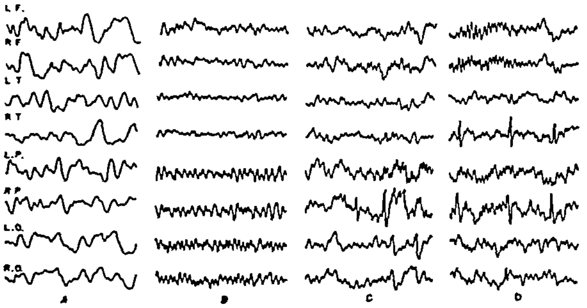

Fig. 8.—Electroencephalographic evidence of subclinical brain disorder produced by measles, with subsequent development of spike focus and clinical epilepsy. *A*, exceedingly abnormally slow electroencephalogram of 7-year-old boy with measles (rectal temperature 100 F); no clinical evidence of brain involvement. *B*, one week later; waking activity returned to normal. *C*, during sleep, focus of spike seizure activity evident in right parietal area. *D*, one year later; patient had two major convulsions in six-month period; condition diagnosed as "epilepsy." Spike seizure activity is present in right parietal and right temporal areas.

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NEW CLINICAL CONCEPT OF SYSTEMIC LUPUS ERYTHEMATOSUS

ANALYSIS OF 100 CASES

Clarence E. Rupe, M.D.
and
Stewart N. Nickel, M.D., Detroit

The case histories of 100 patients with lupus erythematosus were studied for the purpose of identifying factors of greatest value in determining the prognosis. All patients satisfied certain diagnostic criteria, either a positive L. E. cell test result with typical history or else positive biopsy or autopsy findings. In more than half of these patients the survival time exceeded 10 years. Complete remissions sometimes followed treatment or occurred spontaneously. The 34 men in the series were far less seriously ill than the women, less frequently gave a positive L. E. cell test result, and rarely had the classic butterfly rash. When neurological manifestations occurred the prognosis was grave. The least favorable prognosis was in female patients with butterfly rash, systemic involvement, and no arthritis; male patients free from evidence of renal involvement had the best prognosis. Systemic lupus erythematosus in this series appeared to be a more benign disease than was formerly supposed.

The major features of systemic lupus erythematosus have been well known since the early part of the 20th century. Jadassohn,[1] Libman and Sacks,[2] and Goeckerman[3] in particular noted the disseminated character of the disease and reported a wide variety of manifestations. Systemic lupus erythematosus was regarded as a dread and uniformly fatal disease occurring almost exclusively in women. The cardiovascular, arthritic, renal, and systemic toxic features were especially well defined, and the erythematous butterfly rash was considered diagnostic. However, available literature contains little information on benign cases of systemic lupus erythematosus. In addition, few papers on the subject critically correlate specific symptomatology in the disease and prognosis of the patient. It is the purpose of this paper to present a new clinical picture of systemic lupus erythematosus.

The results of this investigation indicate that systemic lupus erythematosus is a more benign disease than previously suspected. It appears to arise from a hypersensitivity reaction. The illness usually follows a chronic course, being more serious

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From the Department of Internal Medicine, Henry Ford Hospital.

in women but common, although mild, in men. The major system involvement appears to be one of the determining factors in the severity and eventual prognosis in patients with the disease.

Method of Study

The medical records of 100 patients at the Henry Ford Hospital with a diagnosis of systemic lupus erythematosus were selected for study. Consecutive cases were examined and the patients chosen on the basis of a well-documented history and physical examination in association with a positive L. E. test result (read by Dr. John Rebuck, Henry Ford Hospital) or biopsy or autopsy findings of lupus erythematosus. The L. E. test gave a positive result in 83% of the patients, 52 women and 31 men. Patients with characteristic systemic manifestations and a positive L. E. cell test result, with at least five L. E. cells, were considered to have lupus erythematosus as defined by a committee of the American Rheumatism Association.[4] Patients with a positive L. E. cell test result, with less than five L. E. cells, were not considered to have the disease without, in addition, either the diagnostic butterfly rash or the characteristic renal findings. This was done to exclude patients with rheumatoid arthritis demonstrating the "false-positive" L. E. cell test result. There were 12 complete autopsies in the series diagnostic of lupus erythematosus. Six had negative and six positive L. E. test results. Exceptions to the above rule were five patients (three with a butterfly rash and two with renal changes) included because of typical history, physical findings, and supporting laboratory evidence of lupus erythematosus who lacked the added diagnostic aid of an L. E. cell test or biopsy. The progress of all patients was followed to the time of writing, except for four who have been lost to follow-up. Each case was analyzed for clinical manifestations, morbidity, natural history from onset, and response to treatment. These various observations, sex of the patient, clinical behavior, and duration of disease, were in turn correlated with each other. Morbidity in this study was graded on the bases of both the course of the disease and the capacity of the patient to live a normal life at the time of review. The grades of function ranged from full activity to incapacitation. Intermediate between these were slightly decreased activity and less than one-half capacity.

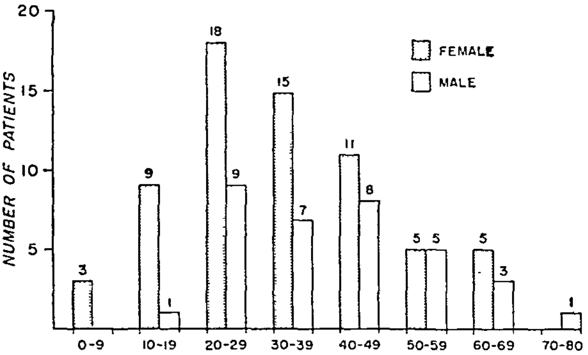

Fig. 1.—Age at onset of disease in 100 patients with systemic lupus erythematosus.

Results

Systemic lupus erythematosus was noted to have a relatively prolonged and generally benign course. The age at onset ranged from 2½ to 74 years and the duration of the disease, as characterized by the onset of symptoms, from 10 months to 36 years (fig. 1). The two-year death rate was 3% while the five-year death rate was 11%. Fifty patients (50%) survived at least 10 years after the onset of the disease, and 45 of these are still living. The benign course was illustrated by the fact that only 2% of the total group proceeded to incapacity. In addition, 58% of the men remained in good health and at full capacity. Fifteen per cent had slightly decreased activity, 12% had less than one-half activity, and no men were incapacitated. In contrast the women were more incapacitated than the men: 26% of the women continued at full activity; 32% were incapacitated to a slight extent; 9% had less than one-half capacity; and 3% were totally incapacitated. There were 25 deaths by the end of the present study, 23 from the disease (19 women and 4 men) and 2 from other causes. Of these patients 14 had survived at least five years from the onset, while 3 patients lived less than two years. The mean survival time in the 25 patients who died was six years from the onset of the disease. Seven of these patients did not receive the benefit of treatment with corticosteroids during their illness. From the above data a classification was made, consisting of three clinical types of systemic lupus erythematosus: (1) chronic continuous, (2) severe intermittent, and (3) acute fulminating. Most patients had the chronic continuous type, which smoldered along with but occasional exacerbation of symptoms. Ten patients had cases that presented a severe intermittent picture, and they died within five years either of progressive renal damage or of fulminating exacerbation. One patient had rapid progression of the illness and died 10 months after onset.

Hypersensitivity in the Pathogenesis of Lupus Erythematosus

The etiological agent in lupus erythematosus was sought by studying events just prior to the onset of the disease. In many patients this was not possible, since the disease had started months to years before the patient was seen here. The description of an instance in which a streptococcic sore throat preceded systemic lupus erythematosus in a young woman follows.

Report of a Case.—A 27-year-old woman was seen in the outpatient clinic with the chief complaint of sore throat of six days' duration. No pleuritic or joint pain was present. Physical examination showed a well-nourished, acutely ill woman, with a temperature of 101.4 F (38.5 C). Her throat and tonsils were moderately inflamed. The rest of the examination was within normal limits. The initial impression was that of a streptococcic sore throat. A culture of the pharynx produced a moderate number of beta hemolytic streptococci. The patient's antistreptolysin titer was 500 units, and the heterophil agglutination test gave negative results. The patient was treated with 1,200,000 units of benzathine penicillin G (Bicillin, long-acting).

The patient had been seen at this hospital seven months prior to the present illness for a preemployment examination and had been found to be completely well. Her history was negative except for an episode of pneumonia at the age of 3 months and a tonsillectomy at the age of 21 years. There was no history of scarlet fever, rheumatic fever, growing pains, arthritis, or allergies. Many injections of penicillin had been given the patient prior to the present illness, without a reaction. Review of systems and family history were noncontributory.

Two weeks after the initial illness the patient returned with a burning, pruritic, plaque-like erythematous eruption over the bridge of the nose and cheeks. There was abdominal cramping and backache. Physical examination showed a typical erythematous butterfly rash over the cheeks. Temperature was 99.2 F (37.3 C) (normal for patient 97.2 F [36.2 C]). Blood pressure was 100/80 mm. Hg and pulse, 80 per minute. Cervical adenopathy was the only additional finding.

Laboratory studies showed hemoglobin level of 11.2 Gm.%; four white blood cell counts ranging from 2,650 to 4,500 per cubic millimeter, with segmented neutrophils 45%, eosinophils 1%, basophils 1%, lymphocytes 45%, monocytes 8%; platelets adequate; and red blood cells normocytic. Serum protein electrophoresis showed total protein content of 7.6 Gm.%, with alpha-1 globulin 5%, alpha-2 10%, beta 12%, and gamma 32% and albumin 42%. Cryoglobulin test result was 2+ in 48 hours, and nonprotein nitrogen content was 27 mg.%. The electrocardiogram and chest x-ray were normal. Result of the L. E. cell test was positive and result of biopsy of a skin specimen was compatible with the diagnosis of lupus erythematosus.

The skin lesion cleared with bed rest. One month later the patient was asymptomatic and thought to be completely well. Result of an L. E. cell test was negative.

Other Cases.—Thirty-three per cent of the patients gave a history of either a sore throat or an earache just prior to their illness. Throat cultures in five of the patients demonstrated beta hemolytic streptococci, alone or together with nonhemolytic streptococci, while in another five a clinical diagnosis of streptococcic throat infection was made, but no culture was taken. In three patients with skin abscesses and in another with a chronic draining osteomyelitis, beta hemolytic streptococci were cultured from the lesions. Other nonspecific infections such as pneumonitis, draining otitis media, cellulitis, carbuncles, and upper respiratory tract infections were noted on occasion to antedate the onset of symptoms. In four patients whose initial illness was felt to be allergic in origin skin testing was done. All were found to have a 2+ to 4+ reaction to beta hemolytic streptococcic, nonhemolytic streptococcic, and pneumococcic protein extracts. In one patient there was a 4+ reaction to histamine, but other skin tests to weeds, house dust, and animal dander gave negative results.

There was a history of some type of allergy in 51% of the patients of this series, 38 women and 13 men. Of this group 16 were sensitive to penicillin, 11 to sulfonamide drugs, 3 to "caine" drugs, and 2 to tetanus antitoxin. In addition, the history of the patients revealed 11 cases of rheumatic fever, 12 cases of scarlet fever, and 3 cases of nephritis. Three of the patients had had toxemia of pregnancy with eclampsia many years prior to the onset of lupus erythematosus. The family of patients in this series often contained a member with one of the collagen or related diseases. Ten patients had immediate relatives with rheumatic fever, 10 with rheumatoid arthritis, 8 with asthma, 6 with nephritis, 3 with what was probably lupus erythematosus, and one each with thrombocytopenic purpura and Raynaud's phenomenon. Nine patients had more than one member of the family involved with one of the above diseases.

Organ Involvement and Prognosis

Most organs of the body were affected to some extent by lupus erythematosus. There appeared to be definite correlation between the organs involved and the prognosis. An erythematous butterfly rash carried a grave prognosis. Of the patients in this series 97% had some type of skin involvement; 38% demonstrated the classic butterfly dermatitis. It seldom occurred in men. There were 34 women (51%) with a butterfly eruption compared to 4 men (12%). Of the female patients with the butterfly rash 11 died, 2 were totally incapacitated, 2 had less than one-half capacity, 8 had slightly diminished capacity, and 11 had full capacity. Two of the males with a butterfly eruption died, one had less than one-half capacity, and one was asymptomatic, with discoid lupus erythematosus. Sun sensitivity was present in 50% of the patients with a butterfly rash, compared to 16% without it. Systemic symptoms were more severe and neurological manifestations occurred oftener in the group with the butterfly rash. Convulsions occurred in six of these patients, psychoses in three, and diplopia in two. Of the patients with the butterfly rash 71% had leukopenia, compared to 43% of the patients without the rash. Of these same patients 42% showed an anemia below 10 Gm. per 100 ml., compared to 25% of those not showing the rash. None of the group of patients with a butterfly rash developed jaundice; however, seven of the patients without a butterfly rash had jaundice, three women and four men. There was biopsy and clinical evidence of posthepatic cirrhosis in three of the men and one of the women.

When neurological manifestations occurred the prognosis was also grave. Eleven patients in the entire series died within five years of the onset of the disease. Of these patients 10 presented neurological symptoms, 7 with severe grand mal convulsions and 3 with psychoses. Progressive azotemia and severe hypertension probably caused the convulsions in five patients, while direct involvement of the brain with lupus erythematosus was the cause in the other two.

The prognosis appeared to be good if the joints were involved with a rheumatoid-like arthritis severe enough to produce x-ray changes or joint deformity. Thirty-one patients fell into this category, 25 women (38%) and 6 men (17%). The average duration of disease from onset in the women was 12 years and in the men 9 years.

Incidence by Sex of Positive Reaction of L.E. Cell Test in Eighty-three Patients

	No. of L.E. Cells, per 500					
	1-4	5-9	10-19	20-49	50-99	100-150
Women (52 patients), % ..	19	27	17	20	11	6
Total, %	46		37		17	
Men (31 patients), %	23	42	22	13	0	0
Total, %	65		35		0	

The presence of kidney involvement was difficult to determine definitely without the aid of a kidney biopsy. The serum nonprotein nitrogen content, results of the phenolsulfonphthalein excretion and urea clearance tests, and intravenous pyelograms are poor aids in the evaluation of renal impairment from lupus erythematosus. However, a urine analysis which on repeated examination demonstrates red blood cells, casts, and albumin is probably the best simple means of detecting any renal abnormality. In the present series 19 men (56%) and 23 women (35%) showed these urinary findings at some period during their disease. Chronic renal insufficiency was determined by a persistently elevated serum nonprotein nitrogen level. Eight men (24%) showed both an abnormal serum nonprotein nitrogen level and abnormal urinalyses, compared to 11 women (16%). Patients with renal involvement appeared to have a fair prognosis. It was only after overwhelming or repeated insults to the kidney that chronic renal failure developed. The duration of the disease from this point to death varied, but some survived as long as five years.

The positivity of the L. E. cell test reaction was compared with the severity of illness in individual patients. It was found that the positivity varied directly with the severity of the illness and the degree of error inherent in counting 500 cells. In a patient with symptoms the L. E. cell test result was usually positive. The number of L. E. cells in each test varied in individual patients with the progression or remission of the disease. The positivity of the test increased in gravely ill patients. Also the difference in the number of L. E. cells found between repeated tests was greater when the L. E. test result was strongly positive. In patients without symptoms the L. E. cell test result was rarely positive.

Sex and Prognosis

The relationship of sex to prognosis, to the L. E. test result, and to the flocculation test result was considered in patients with systemic lupus erythematosus. Of the patients in the present series 34% were men. They frequently developed the disease later in life than the women (fig. 1) and were less incapacitated. The women more frequently developed the disease in their early menstrual life, they were more seriously ill, and the death rate in women was twice that in men. The age at onset of lupus erythematosus showed a striking difference between the men and the women. Although 75% of the cases in each sex started between the ages of 15 and 50 years, the men were evenly distributed throughout the period whereas the women showed a high incidence starting between the ages of 14 to 20 years, with the peak between 20 and 30 years.

Men demonstrated fewer L. E. cells on peripheral blood examination (see table). No man in this series had a positive L. E. cell test result of more than 40 cells, while 17% of the females examined had test results with more than 50 cells. In some cases as many as 148 L. E. cells per 500 cells were counted on a smear.

The cephalin, cholesterol, and thymol turbidity flocculation tests appeared to be a good screening procedure for patients with lupus erythematosus. Of the 73 patients tested 84% showed a positive flocculation test result. The women showed more strongly positive reactions. Of the women 64% demonstrated 4+ reactions, compared to 38% of the men.

Comment

The clinical concept of systemic lupus erythematosus as held by doctors has changed in recent years. Baehr and co-workers,[5] Dubois,[6] and Dameshek[7] considered this a dangerous and deadly disease that occurred almost entirely in women. Jessar and co-workers[8] stated that 20% of his patients survived five years or longer. It was his opinion that the course was short and the prognosis poor in this disease. Other authors such as Harvey and co-workers[9] suggested that systemic lupus erythematosus need not be fatal in every case. A few of their patients were alive many years after the onset of the disease. The present study differs greatly from past reports and offers a new clinical concept of this disease. Systemic lupus erythematosus, in general, is a more benign disease than was previously suspected. The survival time from the onset of disease in this series was at least 10 years in 50% of the patients (fig. 2). Complete remission may occur spontaneously or in response to treatment with anti-inflammatory agents. Three factors seem to account for this changing picture, the most important of which is the diagnosis of benign cases. The second factor is the diagnosis of cases which eventually terminate in death years later. The last factor is the benefit derived from treatment with corticosteroids, which has carried patients over otherwise fatal crises.

Scant reference has been made in the literature to the natural course of systemic lupus erythematosus. Harvey and co-workers[8] stated that systemic lupus erythematosus was characterized by periods of exacerbation and remission which in some cases might last a long period of time. The disease appeared to wax and wane, and a variety of organ systems could be involved at any one time. The waxing and waning nature of the illness was confirmed by the present study. Dameshek[7] felt that a great variation of possible abnormalities could occur in patients with systemic lupus erythematosus. These manifestations varied from time to time and in degree in more or less a random manner. A wide variety of symptoms was noted in the present study and seemed to occur in an orderly sequence. Initially nonspecific symptoms such as fever, weight loss, malaise, mild fibrositis, arthralgia, or abdominal pain might usher in the disease. Later, individual organs such as the kidneys, heart, or joints could become involved with systemic lupus erythematosus. Once these organs were "sensitized" they tended to become involved more easily, with repeated exacerbations of the disease, than did other, unsensitized tissue. Eventually many organs of the body could be affected, rendering the prognosis increasingly more grave in the patient.

One of the most significant findings in this study has been the observation that prognosis and course follow specific organ involvement. It is the type of involvement rather than the degree which is important. The presence of a butterfly rash over the face of a patient with systemic lupus erythematosus was an ominous sign, especially if associated with sun sensitivity, neurological manifestations, or systemic symptoms. The rash was from four to five times more common in women. Both morbidity and mortality were high, and the course was short in this group. In the past the erythematous butterfly rash over the cheeks was the hallmark of the disease. The preponderance of women and the high death rate in previous studies may have been due to the selection of many patients with the easily diagnosed butterfly rash. With increasing awareness of the disease the butterfly rash is seen now in a minority of cases. This may account for the large number of benign cases and the high incidence of men in the present group. It is difficult to speculate beyond this general association of symptoms. In contrast, the presence of a rheumatoid-like arthritis as the main sign of lupus erythematosus improved the prognosis greatly. These patients often followed a long course, extending as many as 25 years from onset. The disease in men tended to fall into remission while women progressively developed joint changes and deformities. Even though synovial changes and symptoms were chronically present in men, they seldom went on to joint deformity. Care was taken to exclude patients with rheumatoid arthritis from this study.

Lately, the renal, hepatic, and hematological manifestations have received much comment. In the present study renal involvement as determined by urine analysis appeared to be more prominent in men. This would be similar to the high incidence of men with acute glomerulonephritis. One patient in the present series was a 20-year-old man, with simulated acute glomerulonephritis as the only manifestation of lupus erythematosus. Results of several L. E. tests on his peripheral blood were strongly positive. This patient might well have been classified as having acute glomerulonephritis, prior to discovery of the L. E. test result.

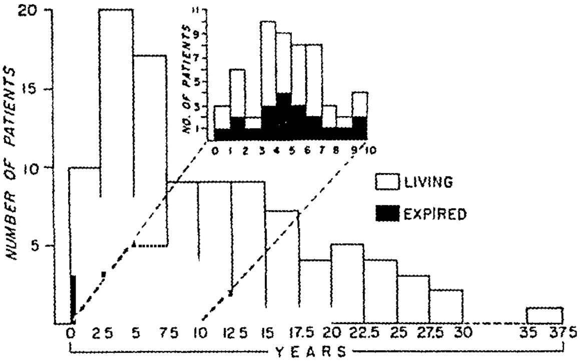

Fig. 2.—Duration of disease from onset of 100 patients with systemic lupus erythematosus.

Chronic renal insufficiency, whether from lupus erythematosus or other causes, always carries a grave prognosis. More than 50% of those who died in the present series had evidence of renal failure. However, many of the living patients did not show any kidney involvement. Renal involvement without insufficiency appeared reversible and carried a fair prognosis. Those who developed chronic renal insufficiency survived for as many as five years.

In a recent publication McCombs and Patterson[10] listed the individual manifestations in 77 patients with systemic lupus erythematosus. From these data several factors were found which influenced the course and prognosis of the disease. The men were severely ill with the disease, although the incidence was very low. Of eight men in this series six died, one had renal insufficiency, and the other was recovering from severe myositis. The authors stated that renal involvement was the most serious prognostic omen. Patients with polyserositis and myocarditis responded to treatment with corticosteroids and their prognosis tended to be good.

The present study does not fully support the conclusions of McCombs and Patterson.[10] The 34 men in the present series were far less seriously ill than the women. The L. E. test result was less often positive in men, and few men demonstrated the classic butterfly rash. The diagnosis was more difficult to make in men than in women. This fact would account for the low number of men recorded in the literature. The rising incidence of men as this study is continued suggests that lupus erythematosus occurs frequently in men.

In spite of the lack of knowledge about the exact cause of lupus erythematosus, certain precipitating factors are generally accepted as being conducive to its development. Infection, drug or sun sensitivity, and cyclic changes in hormones, such as are seen with menstruation, pregnancy, and steroid therapy, are some of the more common ones. A great deal of speculation about the etiology of this disease has been proposed. The endometrium of menstruating women at one time was suggested as a factor in the development of the disease, but no direct evidence was offered for this theory.[7] There is, however, a well-documented report of the occurrence of systemic lupus erythematosus in two patients receiving streptococcus toxin.[11] A definite association was noted between the onset of the disease and the streptococcus toxin. In the present study many of the patients had streptococcic infections just prior to the onset of lupus erythematosus. Throat cultures were positive in five of the patients, while others were described as having a typical streptococcic sore throat. In addition other types of beta hemolytic and nonhemolytic streptococcic infection such as furuncles, abscesses, otitis media, and osteomyelitis appeared to initiate the disease in patients without a sore throat. In some patients prolonged and repeated exposure to these stimuli appeared necessary to initiate the disease. This evidence would give support to a theory that hypersensitivity to streptococci may be an important factor in the disease. Toxemia of pregnancy with eclampsia occurring many years before the onset of lupus erythematosus in three patients in the present series suggests an association to be sought in the future.

The cause of death in patients with lupus erythematosus was either the basic disease process itself or a complicating illness. Harvey and co-workers[9] outlined a variety of causes of death of patients in their series. Among them were acute exacerbation and progressive organ involvement, chemical "causes" without autopsy findings, pulmonary insufficiency, cerebral hemorrhage, renal insufficiency, hemorrhagic tendency, and secondary infection, including pneumonia, endocarditis, and septicemia. Deaths in the present series can be divided into six groups. One, which has not been noted previously in the available literature, is anaphylactoid death. The patient is usually quite ill with multiple organ involvement or in remission from previously severe lupus erythematosus. Without apparent cause there is rapid development of anaphylactoid shock. Acute laryngeal edema and marked dyspnea are characteristic. The patient becomes resistantly hypotensive and convulsions may occur. The toxic manifestations in such a patient may be so overwhelming and prolonged that the patient dies during an acute exacerbation. Chronic renal insufficiency with azotemia was present in 14 patients, 3 men and 11 women. In addition, other serious system involvement often was present in this group. The immediate cause of death was therefore difficult to determine at times. Secondary infections, including pneumonia, accounted for several deaths in this series.

In general, the degree of L. E. cell positivity varied directly with the severity of the disease in individual patients. A more detailed study will be published later. It can be postulated that the L. E. cell positivity reflects the lytic factor in the globulin fraction of the serum protein. This correlation parallels the positivity of the cephalin, cholesterol, and thymol turbidity flocculation tests. The more positive flocculation test results were associated with the more positive L. E. cell tests results and the most seriously affected patients. The women demonstrated almost twice as many 4+ flocculation reactions as did the men.

Summary

Increasing clinical awareness and study of the L. E. cell phenomenon have greatly expanded the understanding of the natural history of lupus erythematosus, revealing its prolonged, frequently benign course. The disease is much more common in men than has been previously reported. The natural history of lupus erythematosus as shown in this analysis suggests a classification of cases into chronic continuous, severe intermittent, and acute fulminating types. The prognosis in the individual case can be more accurately predicted if sex and type of organ involvement are taken into account. In this series a female patient with a butterfly rash, systemic involvement, and no arthritis had the worst prognosis and a male patient lacking evidences of renal involvement had the best. The frequent association of streptococcic infections preceding the onset of lupus erythematosus and re-

peated tissue response in the individual patient suggests a prophylactic possibility. Therapy with steroids may further change the prognosis in lupus erythematosus. At present the apparent increasing incidence of lupus erythematosus and the more frequent recognition of the earlier, milder case make a statistical appreciation of the effects of steroids and treatment difficult.

2799 W. Grand Blvd. (2) (Dr. Nickel).

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LEG BRACING IN HEMIPLEGIA

Kenneth C. Archibald, M.D., New York

Applying braces to the legs in the rehabilitation of hemiplegic patients calls for discrimination. A brace that aids in standing may hinder walking; a patient who needs the knee support of a long brace at first may eventually become able to walk as well with either a short leg brace or none at all. The history of a 61-year-old man after sudden onset of total right-sided paralysis and aphasia illustrates the importance of frequent, apparently minor adjustments in determining the progress of the patient. Bracing is a significant consideration in the management of some hemiplegic patients. When it is necessary, a prompt and judicious choice should be made among devices of the kind here described, and frequent inspection and adjustment may be necessary.

Lower extremity bracing properly applied can improve ambulation in hemiparetic patients. Unnecessarily cumbersome long leg bracing may offer more support and stability during standing but may actually hinder walking. Opinions regarding the indications for different types of bracing vary considerably. This paper will describe the most commonly used types of support for the lower extremities and discuss some of the factors which must be considered before braces are prescribed for adult hemiparetic or hemiplegic patients.

Long Leg Brace

The usual long leg brace[1] consists of two metal uprights, a medial one extending from the ankle joint to a point below the origin of the hip adductors and a lateral one extending from the ankle joint to just below the greater trochanter. Each bar has a hinge at the knee with a lock on the medial upright which enables the patient to unlock the brace with his uninvolved hand. These uprights are held together by two thigh bands and a calf band. The lower ends of the uprights attach to the shoe via a stirrup, or, less desirably, a caliper, plantar flexion being limited either by a rigid posterior "stop," which is usually set at 90 degrees for the hemiplegic patient, or less rigidly by the so-called Klenzak spring joint.

Director of Physical Medicine and Rehabilitation, The New York Hospital-Cornell Medical Center, and Assistant Professor of Medicine (Physical Medicine), Cornell University Medical College.

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There are relatively few indications for a long leg brace in hemiplegia. Only 4 of 60 hemiparetic patients seen during the past three years used long leg braces. Most patients who became ambulatory were eventually able to walk just as well, if not better, with either a short leg brace or none at all. The four patients who required continued knee support to permit walking considered ambulation with the long leg brace too much of a chore to be practical; thus, their minimal ambulation could not be considered functional. In most instances the braces were too heavy and cumbersome.

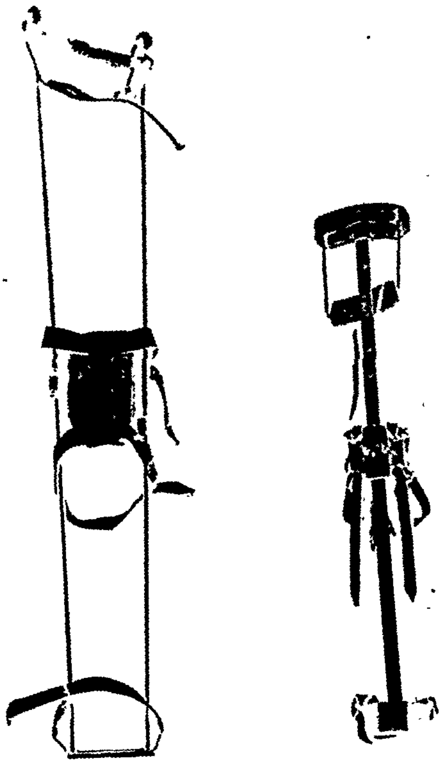

Fig. 1.—Two types of adjustable long leg support for unstable knee.

In the initial training period either an adjustable type of knee support (fig. 1) or a homemade splint made from a newspaper or magazine and held behind the knee by an Ace bandage (fig. 2, *right*) frequently can accomplish the same purpose more effectively and economically. In fact, the amount of posterior support can be more easily regulated by this simple device so that any existing or returning strength of the quadriceps can be utilized more effectively by merely changing the thickness of the newspaper or magazine and adjusting the tightness of the bandage. On the other hand, most types of rigid knee support tend to hold the knee in hyperextension, permitting relatively little action of the quadriceps unless the knee pad is loose, in which case the flexible semirigid quality of support which conceivably serves as an additional exercise stimulus for a weak quadriceps would still not be provided.

Some patients who require hip support initially would benefit by a so-called keystone splint, which is a canvas support containing wooden stays crossing the hip as well as the knee (fig. 2, *left*). The hip straps may be loosened as balance and strength return. Although none of these supports helps the ankle, a piece of strong rubber tubing attached to the front part of the shoe, possibly across the most distal portion of lacing and passing upward to the knee support, will temporarily substitute for weak ankle dorsiflexors during the use of such a device. Of the two adjustable splints shown in figure 1, the lighter single posterior support (fig. 1, *right*) has been more effective, in our experience.

The presence of a knee-flexion contracture constitutes one of the few indications for a long leg brace. In this instance the knee pad is tightened progressively as the flexion contracture decreases. Such bracing is also one method of applying relatively prolonged "knee stretching" either in or out of bed. In one patient a 30-degree knee-flexion contracture was completely reversed and quadriceps strength improved so that a long leg brace was no longer necessary.

Another indication for long leg bracing is a nonunited hip fracture in the hemiparetic extremity, in which case an ischial weight-bearing brace would be necessary. It should be emphasized, however, that it is extremely difficult to make such a brace actually ischially weight-bearing by the use of a Thomas ring. Recently, Russek and Eschen[2] replaced the poorly fitting ischial ring on a long leg brace with a bivalved wooden upper thigh section similar to that used in an above-knee prosthesis for an amputee (fig. 3). Ischial support may also be indicated in the presence of osteoarthritis of the involved knee if there is pain on weight-bearing.[3]

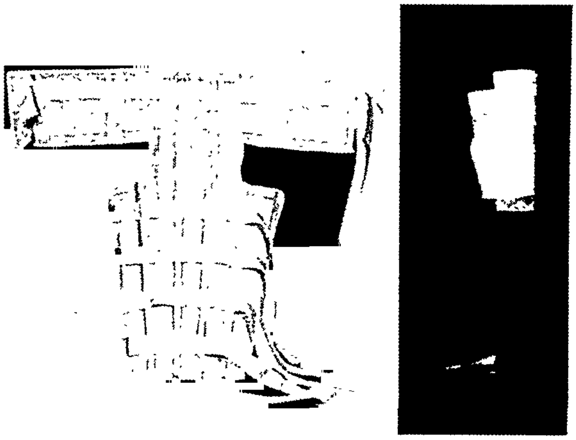

Fig. 2.—*Left*, keystone splint. *Right*, posterior knee support from magazine held in place by Ace bandage.

Short Leg Brace

Short leg bracing is indicated either for lateral instability or when there is insufficient ankle dorsiflexion to keep the forefoot from dragging during swing-through. The classic double-bar short leg brace consists of lateral and medial uprights connected by a calf band just below the knee. The type of ankle joint prescribed becomes increasingly important in the short leg brace, due to its more profound effect on the rest of the extremity and trunk in balance and ambulation.

During the stage of relative flaccidity, a stirrup ankle attachment containing a Klenzak spring joint (fig. 4, *left*) seems most logical for the following reasons. It has been shown [4] that ankle dorsiflexion is strongest on heel strike, in order to prevent the foot slapping that would be seen and heard in the presence of weak ankle dorsiflexors. Electromyographic studies have verified that more strength is required in this lengthening action of the ankle dorsiflexors on weight-bearing than in dorsiflexing the foot during swing-through, an observation long recognized clinically by the early appearance of foot slapping with relatively slight ankle dorsiflexor weakness.

This follows logically, since the ankle dorsiflexors in their attempt at deceleration are opposed by the body weight and its forward momentum at heel strike. With a short leg brace containing a rigid 90-degree ankle stop, this force is suddenly transferred to the calf band, tending to flex an unstable knee until the line of gravity passes anterior to the knee's axis of rotation. If, however, the rigid posterior ankle stop is replaced by a spring which provides less resistance to plantar flexion on heel strike, then the sudden transfer of force to the posterior calf does not occur, unless, of course, the spring is too strong or the brace is set in too much dorsiflexion.

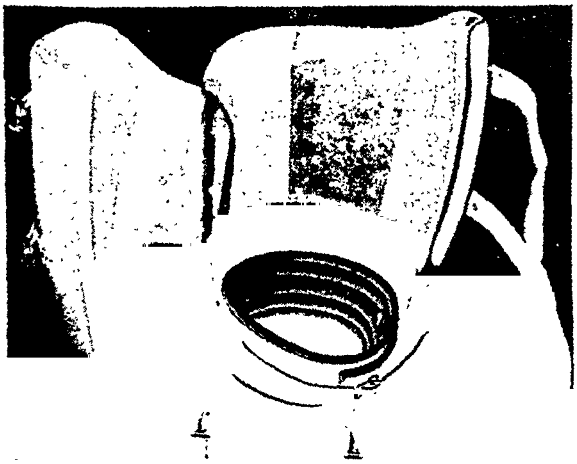

Fig. 3.—Ischial weight-bearing brace with hinged quadrilateral wooden socket.

If a hemiparetic patient has a relatively flaccid ankle and an unstable knee, he may be able to walk with a short leg brace containing the Klenzak spring joint, whereas a rigid 90-degree ankle stop would require posterior knee support or a long leg brace to prevent buckling. Otherwise such a patient would not swing-through but would either swing-to very cautiously or circumduct the leg as a unit, being careful not to place it too far in front of the uninvolved leg.

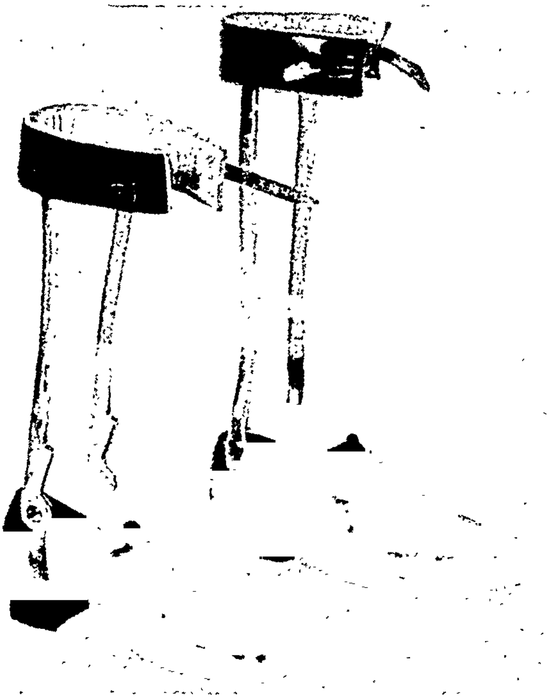

Fig. 4.—Short leg braces with stirrup ankle attachments. *Left*, Klenzak spring joint. *Right*, rigid 90-degree posterior stop.

In these cases use of the so-called intermittent double-step gait, which consists of pausing after every two steps, usually becomes imperative to maintain balance. Peszczynski [5] has emphasized the exaggerated loss of balance occurring during either the stance or the slowed swing phase of the involved lower extremity. In either case such pausing may help prevent this loss of balance and subsequent falling. Also the use of a four-point cane (fig. 5) may be extremely helpful in providing a broader base for better balance.

The following case history illustrates the use of a short leg brace with a Klenzak joint in a patient with a relatively flaccid right-sided hemiplegia, posterior knee support being provided initially by a magazine-type splint.

Report of a Case

A 61-year-old man with a five-year history of hypertension was admitted to New York Hospital. Three days prior to admission while driving home from work the patient had suffered a sudden onset of total right-sided paralysis and aphasia. One day prior to his admission, slight improvement in speech was noted, but the essentially flaccid right-sided hemiplegia persisted. His medical and family histories were noncontributory.

Physical examination revealed the following significant findings: blood pressure 190/105 mm. Hg, pulse rate 84 per minute, and respiration rate 16 per minute. There was a marked expressive aphasia and dysarthria, right homonomous hemianopsia, right-sided lower facial paresis, and a total flaccid paralysis of the upper and lower right extremities. Initially there was a partial right-sided hemianesthesia to pinprick, cotton, vibration, and position sense. Other abnormal right-sided findings included absent abdominal and cremasteric reflexes, an extensor plantar response, hyperactive deep tendon reflexes, but no ankle clonus.

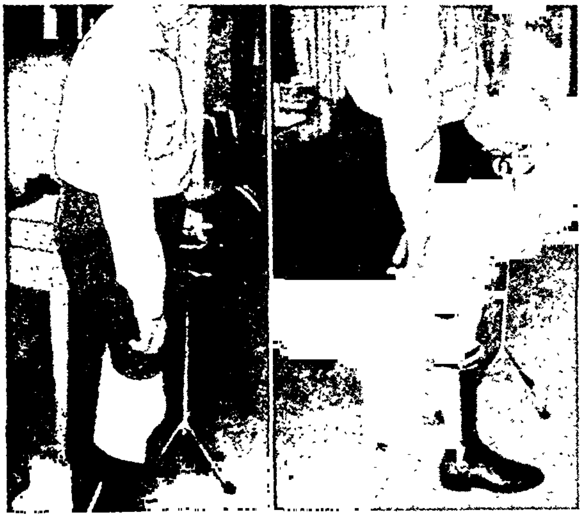
Fig. 5.—Patient with right short leg brace (Klenzak ankle joint) and quadricane. *Left,* with posterior magazine knee splint. *Right,* without posterior knee splinting.

Pulsations of the internal carotid arteries in the tonsillar fossa were strong and equal, and it was felt that the patient had sustained a thrombosis of the stem of the left middle cerebral artery. Laboratory findings, including urine analysis; complete blood count; blood urea nitrogen determination; fasting blood sugar level; and serum sodium, potassium, and transaminase values were essentially within normal limits.

The patient was started on range of motion and active assistive exercises for the right upper and lower extremities and on speech therapy during the first two-week period. After admission there was marked improvement in speech but only slight improvement in strength, so that when balancing and ambulation were first attempted in the parallel bars, with use of an adjustible posterior long leg support, there was still a relatively flaccid right-sided hemiplegia, except for minimal strength in the hip extensor and adductor areas on the right. Initially the trunk balance was extremely poor but gradually improved as did the strength in the trunk and hip areas on the right.

Although the knee extensors remained essentially flaccid, a right short leg brace was ordered. One month after admission the patient was walking outside of the parallel bars in a right short leg brace with a 90-degree Klenzak spring, the knee being supported by a posterior magazine splint (fig. 5, *left*). By the next week he was able to walk without the posterior knee support, using only the short leg brace and a four-point cane (fig. 5, *right*), even though the knee extensors remained relatively flaccid, with a test result no better than "poor." He was able to do this by not allowing weight-bearing on the right lower extremity until his center of gravity was anterior to the axis of rotation of the right knee joint. This was accomplished by his avoiding an excessive swing-through with the right leg and distributing some of his weight to the four-point cane, at least until his line of gravity was far enough forward to prevent his buckling at the right knee. Also he paused for balance after every other step.

Experimental tightening of the spring in the Klenzak ankle joint as well as temporary conversion to a rigid 90-degree stop made walking more difficult because of a tendency toward knee buckling on heel strike. The patient gradually gained increased confidence in this method of walking, which was followed by an increase in the strength of the quadriceps, so that he was discharged on a home program, six and one-half weeks after admission, independent in self-care activities using the left upper extremity to substitute for the severe loss of function in the right upper extremity which remained relatively flaccid. His blood pressure level stabilized at 180-170/100-90 mm. Hg, without the use of any specific hypotensive agent.

Comment

The preceding case report is characteristic of many patients with relatively prolonged flaccidity. In markedly spastic hemiparetic patients, however, a Klenzak spring occasionally tends to induce clonus and additional spasticity. In these patients as well as in those in whom knee extensor strength is good, a rigid 90-degree posterior stop is preferable (fig. 4, *right*). If the involved extremity becomes increasingly spastic, the Klenzak joint may be converted to a rigid 90-degree stop joint by replacing the springs with ball bearings or metal rods. This is not often necessary, however, because, as Machek[6] pointed out, such a problem is physiologically reduced by means of the Weber-Fechner law for discrimination of sensory intensities, the lengthening reaction, and adaptation.

Other types of short leg braces include the posterior spring brace and copper coil brace plus a variety of single bar braces. These may be entirely satisfactory and cosmetically superior for relatively flaccid dorsiflexion weakness, but they are not strong enough for patients with severe spasticity or with severe ankle instability, conditions which may be present without significant weakness in dorsiflexion. In fact, a strong anterior tibial muscle, opposed by weak peroneals, may aggravate a tendency toward lateral imbalance owing to the additional inverting action of the anterior tibial muscle. An appropriate Y-strap on a double bar brace may help to counteract such a tendency. In this situation its base would be attached laterally at the heel and it would be buckled around the medial bar. Also, an outer heel wedge may assist in this situation.

Although no attempt has been made in this paper to discuss the many other important physical and psychological factors involved in ambulation of the hemiplegic patient, obviously one must consider the over-all picture when planning a rehabilitation program. For example, Knapp [3] and Carroll [7] pointed out that a significantly larger group of patients with hemiplegia on the right became more independent than the group with hemiplegia on the left, even though those with hemiplegia on the right may also have been aphasic; this was attributed to greater visuospatial impairment in the group with hemiplegia on the left.

Lowenthal and associates [8] recently reemphasized the need to develop objective criteria for detecting as early as possible after a cerebral vascular accident those patients who would benefit maximally from rehabilitation care. Their feeling was that 65% of the surviving group of 134 patients admitted to Metropolitan Hospital benefited only minimally from rehabilitation care and that improved criteria could enable physical medicine and rehabilitation procedures to be intensified in the remaining 35%.

Bracing constitutes a relatively small but certainly significant consideration in the management of the hemiplegic patient. Decisions concerning this important aspect of the problem should not, on the one hand, be made too hastily or prematurely, nor should bracing be postponed indefinitely to be used only as a last resort.

Summary

Proper bracing in hemiplegic patients can facilitate walking; too much bracing can hinder it. The additional weight of a long leg brace can limit or even prohibit ambulation. Temporary posterior and lateral knee splinting for weak knee extensors can be provided by a folded newspaper or magazine held above an appropriate short leg brace by an Ace bandage.

The type of ankle joint prescribed becomes important when the mechanics of ambulation are considered. If spasticity becomes too severe, a Klenzak spring joint may be easily converted to a rigid 90-degree posterior stop merely by replacing the springs with solid metal rods or ball bearings. Frequent inspection and appropriate adjustment of bracing are essential for the optimal rehabilitation of the hemiplegic patient.

525 E. 68th St. (21).

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OCCUPATIONAL IMPORTANCE OF IONIZING RADIATION.—Even if one considers only the occupational aspect of radiological health, its scope and predictable growth are truly formidable: It is estimated that 175,000 persons are currently employed in atomic energy industry. Thousands of other workers are engaged in operations involving the use of x-rays and radioactive substances. Two thousand hospitals and other institutions are licensed to use radioisotopes for medical purposes. . . . The rapid growth in the past few years in the number of workers dealing with radioactive materials is as nothing compared with the growth we shall see in the immediate years ahead.—David E. Price, M.D., Is Man Becoming Obsolete? *Public Health Reports*, August, 1959.

PROBLEMS AND TREATMENT OF THE CIRCUMILEOSTOMY SKIN

Robert J. McNamara, M.D., Eugene M. Farber, M.D.
and
Samuel I. Roland, M.D., San Francisco

Information about the difficulties which may occur in the skin around the ileostomy outlet was obtained from 451 patients. Dermatitis was reported by 58% of this group; it generally occurred in the early postoperative period (6-12 weeks). The high incidence was ascribed to the prolonged contact of the usually unprotected skin with the ileostomy effluent. The epithelium underlying the ring used to attach the collection bag to the skin was commonly irritated or excoriated by pressure or by adhesive agents. A stoma opening flush with the skin invariably caused irritation, but ileac stumps that were too long were liable to trauma. An ileac stump about 2 cm. in length appeared to be optimal. Karaya powder was reported as helpful by many patients in developing individual techniques of skin care. Many of the patients who had least difficulty in adjusting to and caring for their ileostomies reported "ileostomy clubs" as the best source of help.

Undesirable skin reactions have been observed in the circumileostomy area since the introduction of the ileostomy procedure. In recent years this procedure, with the removal of the entire colon and rectum, has been the preferred operation in the treatment of severe ulcerative colitis.[1] Resultant skin difficulties have been of such severity as to number among the major complications of the postoperative period.[2] Although awareness of its importance in the complete care of the patient has been maintained, the subject of skin care in the ileostomy patient has received relatively little attention in medical literature.

The improvement that has been made in the protection and treatment of the circumileostomy skin can be attributed largely to the mutual cooperation of patients with ileostomies, appliance manufacturers, and surgeons. Through the combined efforts of these persons the care of the patient with ileostomy has steadily improved. In view of necessary therapy for recurring skin difficulties, the dermatologist may occasionally be confronted with skin changes secondary to the ileostomy.

Ileostomy Procedure

Operation.—In order to appreciate the mechanism of action in the changes of the skin accompanying the ileostomy, a review of the surgical procedure and the resultant physiological alteration is necessary. The ileostomy operation entails separation of the gastrointestinal tract at the level of the terminal ileum. Depending on the primary disease, the colon and rectum may or may not be removed. The terminal ileum is brought through a separate incision in the right lower quadrant of the abdomen. The ileac stump is allowed to project a short distance beyond the level of the abdominal skin. In many cases, the stump is matured by removing the muscular layers and folding the mucosa externally to be sutured to the skin of the abdomen.[1a] The resultant intestinal fistula provides a functional outlet for the discharge of intestinal contents. The ileac stump is placed between the anterosuperior iliac spine and the umbilicus, with the operative scar to the left of the midline, enabling the abdominal wall to be free from depression or elevation in this area. This provides a slightly convex abdominal surface for the application of an ileostomy appliance. In order to provide this satisfactory area, it may be necessary to locate the ileac stump elsewhere than in the right lower quadrant of the abdomen.

Discharge.—The ileostomy discharge consists of water, electrolytes, incompletely utilized enzymes, bile secretion, and products of digestion.[3] The hydrogen-ion concentration of the discharge from a normally functioning ileostomy tends toward neutrality or slight alkalinity. In the duodenum the contents are slightly acidic. It has been reported that proteolytic enzymes work best in an alkaline range.[4] The degree of enzymatic activity and hydrogen-ion concentration of the excretion would appear to be related to the activity of the small intestine and the length of time the enzymes are in contact with digestible substrate.

The small intestine is quite active in the immediate postoperative period and discharges a thin, abundant excretion. About six weeks after surgery the discharge begins to thicken in consistency and decreases in amount. During these periods of increased watery discharge, and in diarrhea, the process of complete digestion is impaired, with resultant increase in enzymatic activity in the excretion.

From the divisions of dermatology (Drs. McNamara and Farber) and urology (Dr. Roland), Stanford University School of Medicine. Dr. Farber is now at Stanford Medical Center, Palo Alto, Calif.

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Brooke[5] has shown that the ileostomy discharge need not result in epidermal erosion after contact with unprotected skin. Maceration of the skin after prolonged contact with the liquid discharge, the duration of contact, and the degree of proteolytic activity remaining in the excretion are factors which influence the likelihood of the ileostomy discharge's being harmful to epidermal structure.

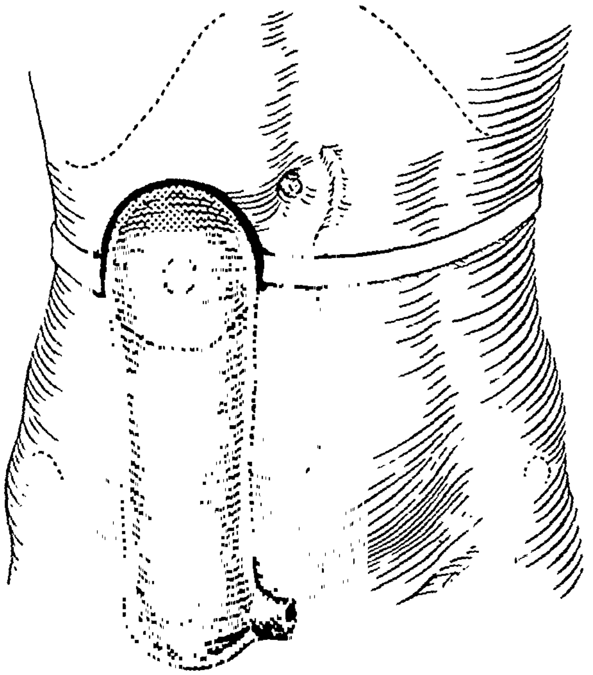

Fig. 1.—Appliance in place over ileostomy stoma. Note location in respect to anterosuperior iliac spine, umbilicus, and surgical scar.

Appliance.—The ileostomy, unlike the colostomy, is actively discharging over a 24-hour period. It is not possible to regulate the excretion by means of irrigation and evacuation of firm, stored feces; instead, a device capable of collecting the semifluid fecal material must be worn. In addition to collecting the excretion, the device must offer protection to the surrounding skin from fecal discharge. The appliance must be worn continually, and many types are available for wear over an extended period of time before changing. Essentially, they consist of a rubber, plastic, or metal disk with a central opening which is placed over the ileac stump (fig. 1). Sufficient room must be present between the inner rim of the disk and the ileac stump to allow for freedom of movement without friction. From the disk is suspended a collecting bag. The bag may be attached separately to the disk or the disk and bag may constitute one unit. The materials used in these appliances vary with the manufacturer. In many instances the appliance manufacturer offers different materials, colors, and designs. Natural and synthetic rubber with added filling agents, plasticizers, accelerators, and vulcanizing agents of lead or sulfur, as well as various types of plastics, comprise the materials of most appliances and collecting bags. Individual variations in design are frequently found, as the patient may alter the proprietary bag to suit his own need; indeed, many patients have designed and built their own appliances.

The collecting bag may be emptied as necessary. Some bags are disposable and may be discarded after use; in other appliances the bag may be emptied through a spout on the dependent end. This is accomplished at a convenient time and place. It is not necessary to remove the disk for this emptying procedure.

In most makes of appliances the disk is designed to be cemented to the skin. Additional support may be gained through the use of a belt which is fitted below the waist, around the hips. Some appliances are designed for the disk to be held by a series of belts without adhesive. Crude rubber or latex with an added solvent such as benzene, n-hexane, naphtha, or carbon tetrachloride make up the basic ingredients of the proprietary adhesives available. To aid in the removal of adhesive when changing the appliance proprietary solvents are frequently utilized.

Recurrent skin irritation in the patient with ileostomy is a distressing and sometimes disabling condition. Severe pruritus, pain, excoriation, and bleeding are seen as a result of chronic circumileostomy irritation. Immediate attention is necessary to avoid prolonged and uncomfortable disability.

Method of Study

There are few patients with ileostomies concentrated in any one geographical area. In order to obtain information concerning the circumileostomy skin difficulties of as many patients as possible, a comprehensive questionnaire was distributed to known patients with ileostomies in the United States and Great Britain (accomplished with the cooperation of ileostomy clubs in the United States and Great Britain). We received a total of 451 replies. In addition, many patients with ileostomies in the San Francisco area were interviewed personally.

Table 1.—*Reason for Ileostomy in 451 Patients*

Disease or Condition	Patients No.	Patients %
Ulcerative colitis	409	90.5
Multiple polyposis	11	2.4
Carcinoma, site not specified	3	0.7
Amebic dysentery	2	0.5
Congenital megacolon	1	0.3
Other	5	1.1
Not stated	20	4.5

Results of Survey

Over 50% of those replying to the questionnaire were in the 30-to-50-year age group. The youngest patient in the group was 11 and the oldest 70 years of age. Four hundred nine patients listed ulcerative colitis as the disease for which an ileostomy was required (table 1). Over 80% had had their ileostomy for at least one year, with two months being the shortest duration and over 34 years being the longest. There did not appear to be a relationship between age of the patient or duration of the ileostomy and the incidence of skin difficulty for the group. Of the 345 patients reporting skin difficulty, 200 (58%) reported that their greatest difficulty occurred during the first six weeks postoperatively. In others difficulty occurred later; in many cases the irritation was recurrent over an extended period (table 2).

TABLE 2.—*Duration of Ileostomy and Period of Greatest Difficulty in 451 Patients*

		Period of Greatest Difficulty													
		0-6 Wk.		6 Wk.-3 Mo.		3 Mo.1 Yr.		1-5 Yr.		Over 5 Yr.		None		No Reply	
Duration of Ileostomy	Patients, No.	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
1-3 mo.	6	3	50	...	...	...	...	...	...	...	...	1	17	2	33
3-6 mo.	15	8	53	4	29	1	6	...	...	...	...	1	6	1	6
6 mo.-1 yr.	58	27	46.5	11	19	9	15.5	1	2	...	...	7	12	3	5
1-5 yr.	238	110	46	32	13.5	33	14	13	5	2	1	29	12.5	19	8
Over 5 yr.	131	51	39	10	7.5	14	11	9	7	6	4.5	20	15	21	16
Not stated	3	1	33	1	33	...	...	...	...	...	...	...	...	1	33
Total	451	200	44.5	58	13	57	12.5	23	5	8	1.5	58	13	47	10.5

Location of Irritation.—A circular area within ½-in. of the ileac stump showed repeated irritation in almost all the patients answering the questionnaire. This is the area of unprotected skin between the inner rim of the appliance disk and the ileac stump (fig. 2). It is necessary that room be allowed for expansion of the ileac stump and for passage of solid objects in the stool. Continuous pressure, as a result of obstruction at the inner rim of the disk, can lead to necrosis of the ileac stump. The amount of irritation may be greater in one location because of variation in the shape of the ileac stump, anatomic defects in the abdominal wall, or an ill-fitting appliance.

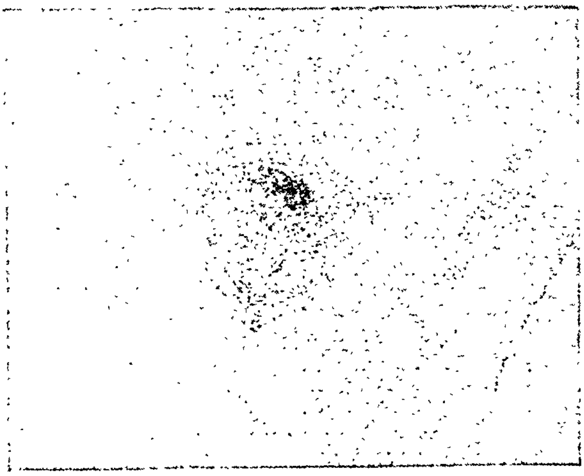
Fig. 2.—Circumstomal ulceration and scar formation in unprotected area between appliance disk and ileac stump.

Repeated exposure to ileostomy fluid occurs in the circumstomal area while the patient is sleeping; this is due to backflow from the collecting bag and pooling of the contents around the ileac stump while the patient is in the supine position. Frequently, the ileostomy disk becomes loosened and seepage of fecal material occurs beneath it, usually in a dependent direction. As mentioned previously, the degree of irritation depends to a great extent on the duration of contact with ileostomy drainage.

The area directly beneath the appliance disk is not infrequently involved (fig. 3). Irritation in this location most often occurs during the first year after ileostomy. The skin apparently is unable to tolerate the various cements and solvents that are commonly used. Intolerance on the basis of an allergic reaction to the materials used in the appliance or cement is rarely found.

It would appear that irritation from adhesive or solvents is due to the primary irritant qualities of the various preparations. Over a period of time the skin directly beneath the appliance disk was noted to become smooth and hyperpigmented; some felt that the skin had toughened and attributed these alterations to repeated changing of the appliance, with application and removal of the cementing substance (fig. 4).

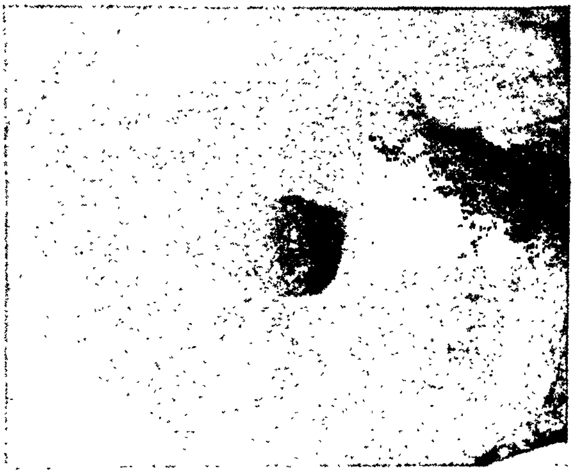
Fig. 3.—Inflammation in area covered by appliance disk. Excoriation from rigid appliance is seen at periphery.

Various difficulties were experienced in the skin not covered by the appliance. These included contact dermatitis of primary irritant and possibly allergic origin (fig. 5), trauma from friction caused by an unyielding appliance disk under the stress of body movement, and repeated adhesive tape application to the outer rim of the disk to prevent early separation of the disk from the abdomen.

Management of Appliances.—A large majority of patients preferred the one-piece or two-piece appliance which could be cemented to the skin. Additional support was frequently used, in the form of a single or double belt. Other methods of holding the appliance in place without cement were used with satisfactory results. Rubber or plastic products were used without preference for either; many patients interchanged appliances and materials to suit specific needs. Size, color, odor, ease of changing, weight, and material were factors which influenced the type of appliance worn. Frequently, several appliances were tried before a satisfactory type was obtained. The best results were reported by persons who were advised and fitted by an ileostomy manufacturer through the cooperation of an ileostomy club.

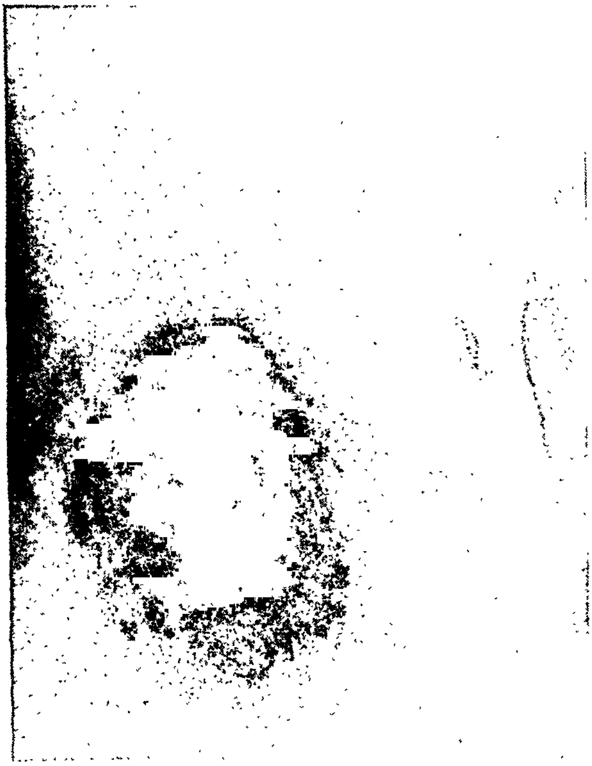

Fig. 4.—Hyperpigmentation, lichenification, and scaling in area repeatedly exposed to solvent and cement.

Most patients preferred to change their appliance at least once a week, frequently daily. Nine per cent changed the appliance more than once a day; in these instances, the type most commonly used was that held in place by straps without adhesive. There was no apparent correlation between the length of time an appliance was worn and resultant dermatitis (fig. 6). Loosening of the disk, foul odor, pruritus or burning, personal hygienic care, and cleaning of the appliance were factors which influenced the length of time an appliance could be worn. Two hundred seventy (60%) said that they changed at a definite time during the day. This usually occurred early in the morning or late at night when the activity of the intestine was said to be at a minimum. Only 20% intentionally waited for leakage to occur before changing the appliance.

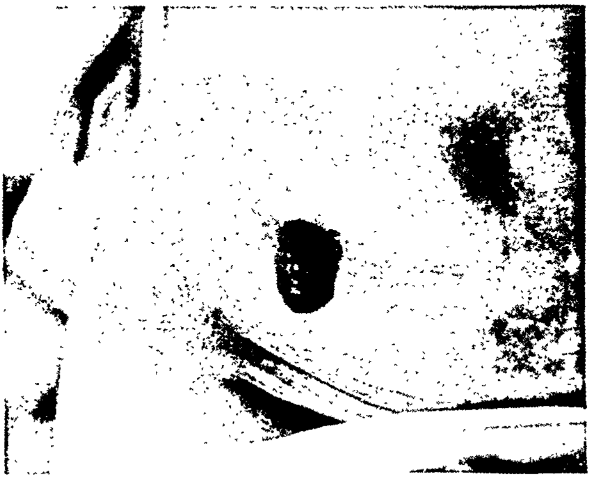

Fig. 5.—Contact dermatitis from use of absorbent gauze pad to collect ileostomy discharge. Appliance was removed because of skin irritation.

Approximately 25% of those replying stated that various factors associated with the ileostomy appliance led to skin irritation. Poorly fitting appliances, bulges or depressions in the circumileostomy area, firm unyielding appliance disks, and a central opening much larger than the ileac stump were among the factors attributed to the appliance or its wearing that contributed to skin irritation. Correction of these difficulties not infrequently led to prompt improvement of the skin problem.

External Factors Influencing Irritation.—Various components in the diet were felt to contribute to skin irritation by 25% of those replying. In general, it was felt that foods or liquids liable to result in diarrhea or those contributing to large, bulky stools were to be avoided. Once the person learned his tolerance for foods and liquids, irritation as a consequence to diet was minimal.

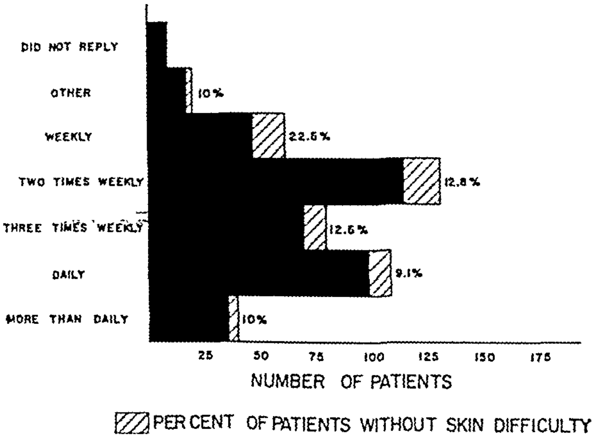

Fig. 6.—Frequency of appliance change, showing number of patients in each group and percentage of group without skin difficulty.

Upper respiratory infection or other illness resulting in diarrhea was liable to cause irritation. Extra care to prevent leakage during these periods of diarrhea decreased the likelihood of irritation.

Temperature variations were found to be of significance only during the warmer periods of the year. Cold weather had no effect on the comfortable wearing of an appliance, but higher temperatures and increased humidity led to early loosening of the disk. This was secondary to perspiration and frequently resulted in some degree of irritation due to leakage of fecal material. Friction of the ileostomy collecting bag on the abdominal wall was also a source of repeated irritation. This was prevented by encasing the collecting bag in a soft "glove-like" cloth and by the use of dusting powders and frequent exposure to air. Increase in odor was also detected during the warm weather. Increased physical activity during the summer months hastened early loosening of the appliance and added to the irritation sometimes found at the periphery of a firm disk as a result of friction.

The length of the ileac stump appeared to be significant only in the extremes. A stoma opening flush with the abdominal skin invariably caused irritation. A long ileac stump was difficult to protect from trauma. Seventy-five per cent of those who replied preferred an ileac stump between ½ and 1 in. in length. The ideal length of the ileac stump has been reported as ¾ in.[6]

The materials used in the appliances, adhesives, and solvents are known sensitizers. Four patients reported an allergic reaction to rubber and two to plastic. These reports have not been verified, but the possibility of an allergic contact dermatitis is certainly within reason. Many reports of intolerance to various preparations are undoubtedly made on the basis of primary irritation. Along with the above products, benzene and tincture of benzoin were mentioned frequently as being irritating. Other preparations were noted to cause irritation less frequently.

The presence or absence of hair in the circumileostomy area was not a factor of importance. Some considered the hair of value in toughening the skin; others felt that the presence of hair was a hindrance and routinely shaved the area.

Revisions.—One hundred thirty-one patients reported at least one surgical revision of the ileostomy; several had more than one revision, one patient reporting five. Five surgical revisions were performed primarily because of skin difficulty. There was a total of 20 revisions to alter the size or shape of the ileac stump. In many instances in which skin irritation had coexisted with such other complications as stenosis of the ileac stoma, retraction or prolapse of the ileac stump, or intestinal fistula, correction of the primary difficulty relieved the skin irritation.

Treatment.—The number of therapeutic agents reported as being of benefit to patients with irritation of the circumileostomy skin was quite large. Proprietary ointments, pastes, and powders containing oil, starch, talc, and zinc oxide were used frequently to relieve acute and chronic inflammation. In general, local therapy followed a routine pattern. Removal of the appliance disk and residual adhesive, usually aided by a solvent, was done with care to prevent excoriation. The area was then cleansed thoroughly, frequently with soap or solvent. If irritation was present, a proprietary salve was applied to the area, care being taken to avoid use of greasy preparations, which might interfere with the adhesiveness of the cementing substance beneath the appliance disk. After a period of exposure to air the disk was reapplied. Changing of the appliance at a shorter interval aided in the recovery of inflamed skin. In a few instances gauze pads were placed over irritated areas. Not only did these pads interfere with adhesion of the disk but they also absorbed fluid and acted as a concentrated source of ileostomy drainage. In spite of increased irritation and prolonged recovery, some preferred to apply solvent and cement over irritated areas. The necessity of wearing a collecting device was the reason these irritants were applied.

Of the various preparations used in the the care and protection of the skin, karaya powder was reported as being of great benefit in the relief of irritation by many patients. This powder is a vegetable gum derivative from the cochlospermum species. Because of its hygroscopic qualities it tends to take up water or serum and form a sticky, somewhat adhesive substance.[7] When allowed to harden it acts as a protective mantle for irritated skin. It is relatively nonirritating and, when properly used, has been reported as effective in the treatment of inflamed areas. In circumstances where cementing substance was contraindicated but the appliance had to be worn over an inflamed area, the karaya powder was sprinkled lightly over the affected site. If sufficient serum was present to form a sticky paste, water was not added; water may be added if the amount of serum is not sufficient. The powder was then sprinkled on the appliance disk and mixed with water to form a sticky film. The appliance disk was then placed over the area of skin which was treated with karaya powder. This supplied adhesive and protective qualities for approximately 24 hours. The appliance had to be changed more frequently with this procedure, but the results were gratifying. Another satisfactory routine for use with karaya powder was to allow the gum to become firm after mixture with water or serum and then cement the appliance on this protective layer. This allowed for slightly longer periods of wear.

Comment

The periods of skin difficulty occurred in two major divisions: the first includes skin difficulty during the first six weeks after surgery, and the second includes skin irritation after the six-week postoperative period.

It is customary to apply temporary ileostomy bags immediately after an ileostomy operation, frequently before the patient leaves the operating room. These consist of disposable units with a double-faced adhesive for application to the abdomen. During the recovery period supervision is necessary to prevent loosening of the appliance and leakage of the thin, profuse ileostomy excretion. At this time of excess discharge tubal drainage of the terminal ileum may aid in controlling overflow.[2]

A permanent appliance should be fitted and applied as soon as the patient is able. Thorough instruction prior to surgery regarding its application and removal is of great benefit in teaching the patient to care for his own appliance at an early stage. Instruction in these matters is best conducted by another patient with ileostomy. Care must be taken at this time to avoid irritation of the circumileostomy skin by primary irritants. Judicious use of solvent and adhesive is recommended, as well as changing of the appliance at the first sign of leakage or loosening.

Improvement in the patient's physical status and the slowing down of the ileostomy discharge at the end of six weeks is reflected in the decreased incidence of skin difficulty at this time. The patient tends to gain weight, filling out depressions on the abdominal wall, and refitting of the appliance may then become necessary.

Ideally, the wearing of a proper appliance and normal supervision should be sufficient to prevent circumileostomy irritation. As mentioned previously, other factors contribute to the development of irritation in the course of the life of a patient with ileostomy. It would seem apparent that prolonged contact of the ileostomy discharge with the unprotected skin of the abdomen is the exciting cause of most irritation. The macerating effect of the fluid and the potentially corrosive properties of substances it contains are sufficient to initiate the irritation. Repeated irritation or aggravation by solvents or adhesives tends to exacerbate the inflammation. In order to protect the epidermis from these irritants adequate supportive measures should be taken.

To aid in forming a comfortable base for the appliance disk and to give more protection to the unprotected area between the disk and the stoma, a foam rubber pad may be placed between the appliance disk and the abdomen. This foam rubber contains closed pores and is not absorbent, as is sponge rubber.[8] The rubber disk extends beyond the appliance disk peripherally and closer to the stoma centrally; its soft consistency prevents the peripheral irritation caused by a firm disk and affords more protection from the ileostomy discharge in the circumstomal area. The rubber pad is first cemented to the skin and then the disk is cemented to the pad; this allows the patient to observe the fitting of the inner ring over the ileac stump with more accurate placement.

As mentioned above, karaya powder is effective when used properly and aids in relieving slight irritation, when it is substituted for adhesive. Replacing old appliances and refitting to allow for body changes is important in preventing leakage. Changing of the appliance at the first sign of leakage is mandatory. Leakage should not be depended on as a sign for changing the appliance; rather, the patient should develop a routine interval for care of the ileostomy.

In cases of recurrent irritation over a prolonged period of time, the possibility of an allergic reaction to one of the materials being used should certainly be investigated. When primary irritants are found to be the cause of repeated irritation, discontinuing or diluting the offending agent may be all that is necessary to relieve the irritation.

Surgical correction of ileostomy malfunction aids in treating an existing skin difficulty. Attempts to treat skin difficulty in areas of repeated exposure to irritating substances are futile. In our hands, simple local therapy for inflammation was satisfactory, providing the ileostomy discharge could be collected and no irritating preparation was used.

It was significant to note the improvement in these patients by the mutual association which they enjoy through organized ileostomy clubs. Advice on ileostomy appliances and care is available through these organizations. Once the patient has learned to care for his ileostomy in a satisfactory manner, skin problems become less serious.

Summary

A comprehensive questionnaire concerning the occurrence of circumileostomy skin difficulties was sent to patients with ileostomies in the United States and Great Britain. Of the 451 patients replying 345 (76%) reported skin difficulty of varying degrees since operation. Over 50% reported that skin difficulty was most severe during the first six weeks after ileostomy.

The most common site of skin irritation was a circular area within ½ in. of the ileac stump. This area is constantly exposed to the semifluid ileostomy discharge. Another area of frequent irritation was the skin directly beneath the appliance disk and, infrequently, at the periphery of the disk. Maceration of the skin after prolonged contact with the liquid discharge, the duration of contact, and the degree of proteolytic activity remaining in the excretion were factors which influenced the likelihood of the ileostomy discharge's being harmful to epidermal structures. The use of adhesives and solvents associated with the application and removal of the ileostomy appliance also influenced the degree of irritation. The materials used in the manufacture of the ileostomy appliance rarely contributed to circumileostomy irritation.

Poorly fitting appliances, bulges or depressions in the circumileostomy area, unyielding appliance disks, and a central opening much larger than the ileac stump were among factors that contributed to skin irritation. Correction of these mechanical and anatomic difficulties not infrequently led to prompt improvement of the skin problem. Ileostomy stump complications such as stenosis, retraction, or prolapse frequently resulted in secondary skin changes. Correction of these surgical complications was necessary in order to relieve the skin irritation.

Secondary factors must be corrected before adequate treatment is instituted. Karaya gum powder is recommended for use in treating patients who need an adhesive and protective substance in order that the appliance may be worn over an inflamed area. Leakage should not be depended on as a sign for changing the appliance, and old or poorly fitting appliances should be replaced in order to prevent leakage.

Considerable improvement was seen once the person had learned to care for his ileostomy in a satisfactory manner. Association with an ileostomy club was of great benefit in providing individual instruction for care of appliances.

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SURVEILLANCE AND CONTROL OF STAPHYLOCOCCIC INFECTIONS IN A MATERNITY UNIT

Sanford M. Farrer, M.D., Philadelphia, Richard Russo, M.S.P.H., Camille Bavara, R.N., Trenton, N. J.
and
Seymour Werthamer, M.D., Lakewood, N. J.

An 84-bed community general hospital with approximately 4,000 admissions and 750 live births per year became aware of a problem of staphylococcic infections when a 2-day-old baby developed a paronychial abscess. During the ensuing seven days 11 newborn infants were found to have pustular lesions yielding similar organisms. The nursery was closed temporarily, and extraordinary efforts were made to eradicate all sources of infection and to eliminate errors of technique. Improvement was only temporary, and the epidemic reached a second peak in June, 1958, when 29 (60%) of 48 deliveries successfully followed-up were found to be associated with suppurative infection. Among the measures that were tried, the one that seemed to contribute most to the termination of the epidemic was compulsory rooming-in of the infant with the mother.

During recent years outbreaks of staphylococcic infections among newborn infants and postpartum mothers have been reported in the literature with increasing frequency. These reports have come from widely scattered areas of the world. In August, 1957, Shaffer and associates[1] reported 19 nursery epidemics in the United States, Canada, and Australia caused by an identical strain of Staphylococcus pyogenes var. aureus. An epidemic of staphylococcic skin lesions, maternal breast abscesses, and infant "sticky eye" was reported by Monro and Markham[2] from New Zealand, in 1958. Gillespie and Alder[3] described an outbreak of neonatal pemphigus in England which was attributed to spread from a single nasal carrier of a strain of

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Member of the Epidemic Intelligence Service, Communicable Disease Center, U. S. Public Health Service, Atlanta, Ga. (Dr. Farrer); member of the staff of Maternal and Child Health Programs, Division of Constructive Health, New Jersey State Department of Health (Mr. Russo); Public Health Nurse Consultant, Hospitals, Maternal and Child Health Programs, Division of Constructive Health, New Jersey State Department of Health (Miss Bavara); and pathologist at the Paul Kimball Hospital, Lakewood, N. J., and Deborah Hospital, Browns Mills, N. J., and Instructor in Pathology, Seton Hall College of Medicine and Dentistry, Jersey City (Dr. Werthamer). Dr. Farrer is assigned to the Department of Research Medicine, University of Pennsylvania.

Staphylococcus aureus. Timbury and associates[4] recently reported a staphylococcic epidemic in a maternity hospital in Scotland. In the United States, reports of staphylococcic epidemics among newborn infants and their mothers have originated from Seattle[5]; Ohio[6]; Columbia, S. C.[7]; Galveston, Texas[8]; Lincoln, Neb.[9]; and Ridgewood, N. J.[10] Many of these outbreaks have been attributed to a single strain of Staphylococcus aureus, phage type 80/81.[11] The world-wide distribution of this particular strain and its propensity to cause infection in newborn infants has caused many persons to refer to it as the "hospital" or "epidemic" strain of Staphylococcus aureus.

The purpose of this paper is to record the problems encountered during an outbreak of staphylococcic infections among newborn infants and their mothers in a small community hospital, the methods used to investigate the nature and extent of the epidemic, and the measures adopted to control it.

The Paul Kimball Hospital, Lakewood, is an 84-bed general institution, located in the eastern part of the state of New Jersey. It serves a community of approximately 16,000 persons, composed of a resident population principally engaged in the tourist trade and poultry farming and a transient tourist and military population. The number of admissions to this hospital is approximately 4,000 per year; the number of live births is approximately 750 per year.

The full-term nursery, adjacent to the maternal postpartum unit, consisted of one room which housed from 10 to 20 bassinets, depending on fluctuations in census. Frequently, because of overcrowded conditions, the desirable minimum of 24 sq. ft. of space for each infant was not available. Adjacent to the full-term nursery was a small work room which permitted access to a nursery for premature babies which was large enough to accommodate two infants. Formula preparation rooms and utility and circumcision facilities were provided in other parts of the maternity unit. Dressing rooms for nursing and medical personnel were not available.

The Epidemic

The staff became aware of a problem of staphylococcic infections in the nursery on Oct. 5, 1957, when a 2-day-old baby developed a paronychial abscess. Within the succeeding six days five newborn infants developed pustular skin lesions on the face and trunk. On Oct. 18, the "index" infant with the paronychial abscess was readmitted for incision and drainage of a breast abscess which, on culture, yielded Staphylococcus aureus, coagulase-positive. During the ensuing seven days 11 newborn infants were observed to have pustules, all of which yielded coagulase-positive Staphylococcus aureus. On Oct. 25 the nursery was closed, thoroughly cleaned, and repainted. All babies born between Oct. 25 and Oct. 29, 1957, were admitted to a temporary nursery converted from a postpartum ward. On Oct. 30, 1957, the original nursery was reopened. Despite these attempts at control of the epidemic by closure of the nursery, newborn infants continued to develop staphylococcic infections.

At that point the hospital requested assistance from the New Jersey State Department of Health. A joint project was undertaken by the hospital staff, the New Jersey State Department of Health, and the Communicable Disease Center (U. S. Public Health Service) to investigate the source, nature, and extent of the outbreak and to institute measures to terminate it.

Methods and Materials

Morbidity Survey.—Three methods were used to secure morbidity data on all mothers and infants delivered at the hospital from September, 1957, through January, 1959. All hospital charts and all bacteriological records were reviewed, and mothers who could be reached by telephone were called approximately six weeks after discharge. Information obtained from the chart, such as the obstetrician's name and the dates of delivery and discharge, promoted confidence of the mother in the telephone investigator and permitted free and easy discussion of the following topics: whether the infant was breast-fed or bottle-fed; whether the infant, mother, or other family members had experienced suppurative illness since discharge from the hospital and, if so, the nature, date of onset, severity, duration, and treatment of such illness. If a mother was unable to be reached by telephone, her obstetrician was asked to secure morbidity information.

Bacteriology.—Cultures from lesions, from the nose, skin, and vaginal tract, and from inanimate objects were obtained by means of unmoistened, sterile cotton swabs. The swab was introduced immediately into thioglycollate broth and then inoculated on blood-agar plates. After 24 hours' incubation at 37 C, isolation of staphylococci was attempted. Isolated colonies were tested for coagulase production by standard tube methods, with use of citrated human plasma.[12] Coagulase-positive staphylococci were transferred to fresh agar slants and forwarded to the division of laboratories of the New Jersey State Department of Health for bacteriophage-typing with 25 standard phages by the method of Williams and Rippon[13] and Blair and Carr.[14] Antibiotic sensitivity tests were performed by the disk method, by means of medium concentration Difco disks of the following strengths: chloramphenicol (Chloromycetin), 5 mcg.; dihydrostreptomycin sulfate, 10 mcg.; erythromycin, 5 mcg.; nitrofurantoin (Furadantin), 150 mcg.; penicillin, 5 units; oxytetracycline (Terramycin) hydrochloride, 10 mcg.; and tetracycline, 10 mcg. Sensitivity to an antibiotic was graded qualitatively, by observation of the presence or absence of a zone of inhibition to a particular drug. Air cultures were obtained by exposure of blood-agar plates to the air for one hour.

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Month	Live Birth Deliveries	Post-discharge Follow-up Completed*	Associated with Suppurative Infection No.	%†
1957				
Sept.	48	34	9	26.5
Oct.	57	50	28	56.0
Nov.	83	71	36	50.7
Dec.	69	54	29	53.7
1958				
Jan.	88	74	28	37.8
Feb.	41	33	5	15.2
Mar.	64	55	4	7.3
Apr.	46	30	5	16.7
May	67	47	4	8.5
June	61	48	29	60.4
July	73	55	22	40.0
Aug.	64	60	5	8.3
Sept.	52	47	2	4.3
Oct.	67	57	4	7.0
Nov.	..	..	..	....
Dec.	63	57	2	3.5
1959				
Jan.	56	45	2	4.4
Total	1,009	817	214	26.2

* 19% of mothers and newborn infants were lost to follow-up.
† Based on deliveries with completed follow-up.

Review of Practices, Policies, and Procedures.—A thorough review of the procedures, practices, and techniques applied to newborn infants and their mothers was undertaken by a trained public health nurse consultant with many years of experience in obstetric nursing practices. Detailed observations of techniques in labor and delivery, postpartum care, and the nursery were recorded.

Results

Case-finding Methods.—A telephone survey proved to be an efficient, accurate, and rapid method for collecting data on staphylococcic morbidity in newborn infants and their mothers after discharge from the hospital. Sixty-four per cent of the mothers discharged from the hospital during a 16-month period were reached by telephone. The average length of time for each call was approximately seven minutes. Not a single mother voiced objection to the survey or refused to discuss the health of her infant with the investigator. Moreover, no legal repercussions or adverse journalistic publicity resulted from the telephone survey. Postpartum mothers are usually sufficiently concerned about the health of their infants to cooperate willingly in surveys of this type.

Positive cases of infection were accepted as such only if the mother's description of the lesion included purulent exudate. Doubtful cases were excluded unless confirmed by the family physician. Evaluation of staphylococcic infection by telephone may be difficult, but in most cases the description of the lesions left little doubt about the diagnosis. Even less doubt was entertained about the accuracy of the telephone survey as a case-finding method when it was discovered that in 87% of the "phone survey cases" infants were treated by physicians for their disease. Moreover, many of the infants classified as positive by the telephone investigators were also reported by physicians, and a number of them were admitted to the hospital for treatment. Thirty-six per cent of the mothers could not be reached by telephone. Follow-up information on them was sought by questionnaires sent to their physicians, but this procedure was successful in only 17%. Nineteen per cent were lost to follow-up completely, because they were without telephones, had moved from the community, or had not returned to their physician since delivery.

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The over-all rate of staphylococcic infection during the 16 months of survey was 25.6% for infants and 3.7% for mothers. During the "epidemic" period the rates of attack were 37.5% for newborn infants and 5% for mothers; during the "nonepidemic" period 5.1% for newborn infants and 1.4% for mothers.

TABLE 2.—*Types of Staphylococcic Infections in Obstetric Unit*

Illness	Infants	Mothers	Total
Cutaneous	169	23	192
Cutaneous and conjunctivitis	18	1	19
Cutaneous and breast abscess	9	0	9
Cutaneous and other	2	0	2
Conjunctivitis	8	1	9
Breast abscess	2	4	6
Other abscess	1	1	2
Bronchopneumonia	2	0	2
Total	211	30	241

Types of Infection.—The types of staphylococcic infection which occurred are listed in table 2. Cutaneous staphylococcic disease, principally of the pustular type, was the most common manifestation among both infants and mothers and accounted for 80% of the infections. An additional 12% of the infections were combinations of cutaneous and other manifestations. The remaining 8% consisted of breast abscesses, purulent conjunctivitis, bronchopneumonia, and other miscellaneous illnesses. The four maternal breast abscesses occurred in mothers who were breast-feeding their infants prior to or at the time signs of infection developed. One of the two infants who developed staphylococcic bronchopneumonia died; coagulase-positive staphylococci were cultured from his lung.

Table 3.—*Time of Onset of Staphylococcic Lesions in Obstetric Unit*

	No.	%
Infants infected	211	
Onset before discharge	72	34.1
Onset after discharge	139	65.9
Mothers infected	30	
Onset before discharge	2	6.7
Onset after discharge	28	93.3

Etiology of the Epidemic.—Microbial cultures were obtained from 76 lesions during this 16-month period. The majority of these were from infections in newborn infants which occurred before discharge from the hospital. Sixty-three cultures yielded staphylococci whose principal characteristics were coagulase production, hemolysis, yellow pigment production, and a high degree of antibiotic resistance. Twelve cultures showed no growth. One culture revealed a gram-negative micro-organism. Of the 63 staphylococcic cultures obtained, 47 (74.6%) were typable with standard bacteriophages, and 41 (65.1%) were type 80/81, a strain which is probably identical to the "epidemic" strain mentioned above and reported by numerous investigators throughout the world. Ninety-two per cent of the staphylococcic strains typed as 80/81 were resistant to penicillin, 80% to dihydrostreptomycin sulfate, 88% to oxytetracycline hydrochloride, 73% to tetracycline, 70% to erythromycin, 35% to chloramphenicol, and 35% to nitrofurantoin.

When coagulase-positive staphylococci, obtained from lesions and noses, of phage patterns other than 80/81 were examined for antibiotic sensitivity, a slightly different pattern evolved. The percentage of resistance was as follows: penicillin 70%, dihydrostreptomycin sulfate 70%, oxytetracycline hydrochloride 75%, tetracycline 80%, erythromycin 25%, chloramphenicol 59%, and nitrofurantoin 52%.

Onset of Infant and Maternal Illnesses.—The importance of establishing a case-finding system which will record suppurative disease in infants and mothers during the immediate posthospitalization period, as well as during hospitalization, is borne out by the data in tables 3 and 4. Of the 211 infants with clinical suppurative infections 139 (65.9%) experienced the onset of signs and symptoms of infection after discharge from the hospital, and the lesions occurred from 1 to 68 days (median, 7 days; mean, 10.6 days) after delivery. Breast abscesses occurred from 1 to 17 days (median, 7 days; mean, 8.2 days) from the day of delivery, and one case of neonatal staphylococcic bronchopneumonia occurred 30 days after delivery.

The figures in tables 3 and 4 significantly point to the even greater need to follow up the posthospitalization incidence of cases of suppurative infections in mothers. Twenty-eight (93.3%) of the 30 infected mothers experienced onset of disease after discharge from the hospital. The average time from delivery to onset of infection was 28 days and the median time interval, 25.5 days.

Survey of Microbial Cultures.—Cultures were obtained from infants, mothers, hospital personnel, and the hospital environment.

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The correlation between nasal cultures obtained from newborn infants on discharge from the hospital and the development of clinical staphylococcic infection is as follows. Of the 33 infants infected by the "epidemic" strain phage type 80/81, during an eight-month period, 14 (42.4%) developed suppurative infection. On the other hand, only 7 (11.1%) of the infants infected by other coagulase-positive staphylococci before discharge developed such infection.

Mothers: Of the nasal swabs obtained from 64 mothers on admission, 13 (20%) yielded coagulase-positive staphylococci, only one of which was phage type 80/81. On discharge from the hospital 10 (17.2%) positive cultures were obtained, and 3 (5.2%) of these were type 80/81. The fact that none of the mothers of infants with type 80/81 nasal or umbilical cultures carried this strain suggests that the mothers were not the source of infection for their own infants while in hospital. Thirty-two cul-

Table 4.—*Interval, Delivery to Onset, of 170 Staphylococcic Infections in Obstetric Unit*

	No. of Infections	No. of Days		
		Mean	Median	Extremes
Infant (all infections)	158	10.6	7.0	1-68
Cutaneous	131	10.5	7.0	1-68
Conjunctivitis	16	9.4	5.0	1-67
Breast abscess	8	8.2	7.0	1-17
Abscess, other site	2	19.5	19.5	12-27
Bronchopneumonia	1	30.0	....	.....
Maternal (all infections)	12	28.1	25.5	12-75
Cutaneous	7	28.1	18.0	12-75
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Breast abscess	4	26.0	27.0	20-30
Abscess, other site	1	36.0	....	.....

tures were obtained from the vaginal tract of mothers just prior to delivery. Only 2 (6.2%) were coagulase-positive, and none was type 80/81.

Personnel: Anterior nasal swabs were secured from 112 personnel who maintained working contact with the nursery-maternity unit. From persons who carried coagulase-positive staphylococci additional cultures were obtained on two successive occasions, not less than one week apart. As a result of this procedure, "persistent" carriers of type 80/81 were identified. "Persistent" carriers comprised 14% of the total hospital population and included nine physicians, five nursing service personnel, one laundry employee who folded clean linen for the nursery, and one housekeeping employee.

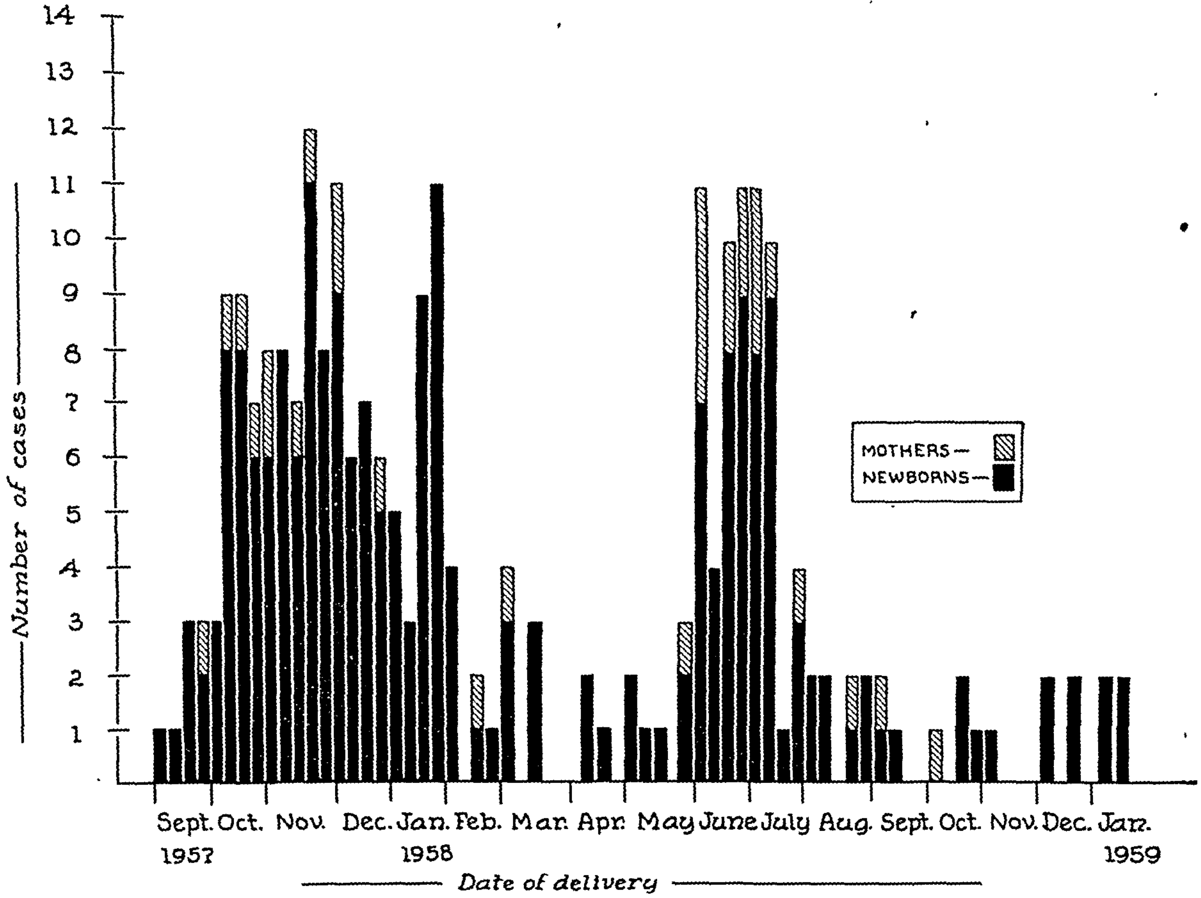

Fig. 1.—Staphylococcic epidemic in maternity unit: reported cases.

Environment: Sixty cultures were obtained from floors, walls, bassinets, work tables, blankets, doorknobs, and air in the nursery and the delivery rooms. The air-settling plates were placed in the nursery during periods of maximal activity. Only two cultures yielded staphylococci of phage type 80/81, and both were settling plates exposed on the same day in the nursery.

Control Measures.—The high rate of morbidity in newborn infants suggested that staphylococci were being transmitted through the nursery with relative ease. Although the survey of microbial cultures, conducted from November, 1957, through January, 1958, did not define the manner of transmission, it did succeed in identifying 16 persistent carriers of phage type 80/81 among the personnel on the nursery-maternity service. This finding suggested that the reservoir of pathogenic staphylococci existed among the staff and that the perpetuation of the epidemic might be related to the presence of nasal carriers. Accordingly, initial control measures were instituted in January, 1958, which were directed toward breaking the chain of transmission from infant-to-infant and from infant-to-personnel-to-infant.

Nursing and housekeeping personnel who were nasal carriers of staphylococcus type 80/81 were removed from the nursery-maternity unit and given employment in less critical areas of the hospital. The laundry employee was removed from the clean linen room. Physician-carriers observed the following regimen: they carried out double scrub of the hands before delivery; they wore double face masks in the delivery room, changing masks every 30 minutes; and they were excluded from the nursery proper and did not handle infants after delivery. All employees underwent physical examination for the detection of pyogenic lesions, and the importance of reporting such lesions to the chief nurse was emphasized. However, no employees with overt cutaneous or respiratory staphylococcic lesions were discovered.

Since it has been demonstrated that infants are more likely to be infected by staphylococci after the 3rd hospital day of life, a new uniform discharge policy was adopted which directed that infant and mother be discharged on the third day after delivery except in the case of complications.[15] Because nursing mothers tend to develop breast abscesses more often than non-nursing mothers, breast-feeding of infants was discouraged for the duration of the epidemic.

Subsequent to an exhaustive survey of techniques, practices, and procedures many changes were effected which improved the quality of asepsis. Handwashing regulations were adopted for all personnel, and the importance of washing each time before caring for each newborn infant was emphasized. Provision of an adequate supply of clean gowns, dresses, and masks was insured. In the nursery, nurses were required to wear scrub dresses, and all transient personnel, including physicians, were required to wear gowns, caps, and masks. Common equipment for the care of newborn infants was eliminated, and, whenever feasible, each infant was given individual medicinal supplies, laundry packs, and instruments. Unnecessary dust-collecting nursery equipment was eliminated. Covered, foot-controlled waste receptacles were provided. Wet-mopping of floors and damp-dusting were instituted, together with the adoption of a phenolic germicide for surface cleansing. A "nursery-to-house suspected cases of infection" service was established, and facilities for isolation of newborn infants and mothers with staphylococcic lesions were provided.

The course of the epidemic is shown in figures 1 and 2. A decrease in infection occurred after the institution of the above control measures in January, 1958. These control measures were maintained during the spring of 1958, and close surveillance of infants before and after discharge was continued. Despite these precautions, a second wave of pustular skin diseases occurred in June, 1958. The reasons for this second wave were not defined. None of the previously identified carriers had been reintroduced into the nursery, and none of the mothers who had been in the hospital during the first epidemic period was readmitted. In July, 1958, a second set of control measures was introduced, which included closing of the full-term nursery and institution of compulsory rooming-in of the infant with its mother, periumbilical painting with triple dye (brilliant green 2.3 grains [138 mg.], gentian violet 2.3 grains [138 mg.], acriflavine 1.1 grains [66 mg.], water 1,000 ml.), and administration to the baby at birth of 0.1 cc. of gamma globulin per pound of body weight. The latter two measures were soon discontinued, but compulsory rooming-in of infants has been maintained since July, 1958. With the institution of rooming-in a significant fall in infection occurred. Whereas, during the nine and one-half–month period prior to rooming-in the number of deliveries associated with staphylococcic infection had been 37.1%, it was only 6.8% during the five and one-half–month period since the establishment of rooming-in.

Comment

In appreciation of the fact that newborn infants may develop signs and symptoms of staphylococcic infection in the immediate period after discharge from the hospital and that the maternity hospital may be the source of infection for the newborn infant, his mother, and, in some cases, other family members, many hospitals have established organized systems to follow the health of infants during the neonatal period. Murray and co-workers[7] found that the interval from delivery to onset of suppurative illness in the infants studied in one epidemic ranged from 3 to 33 days, with a median interval of 9 days; the bulk of maternal breast abscesses occurred from 12 to 18 days after delivery, with a median interval of 16.5 days. Wysham and associates[5a] reported that the median interval for infants in a Seattle hospital was six and the mean interval eight and one-half days. In this outbreak of infection skin lesions in infants occurred from 1 to 68 days and four breast abscesses in mothers between 20 to 30 days after delivery. Thus, it seems imperative that infants and mothers be followed up for at least six weeks after delivery if one is to ascertain the true nature and extent of the problem of staphylococcic infection in a hospital.

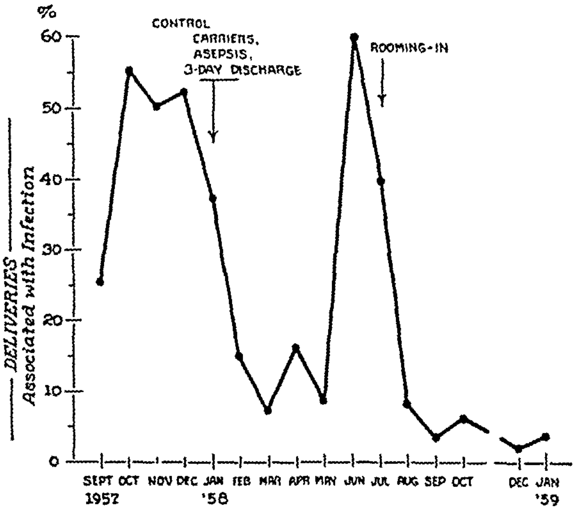

Fig. 2.—Effect of control measures on course of staphylococcic epidemic in maternity unit.

Several systems have been used by hospitals to check the health of newborn infants and mothers after delivery, such as sending questionnaires to the attending physician, or to the mothers themselves, and visits to the home by public health nurses. In the present outbreak the telephone survey among mothers evolved as the single most important case-finding device. The average time per telephone call was seven minutes. Refusal to answer the questions posed by the investigator was not encountered in a single instance out of 648 calls. In fact, in several cases mothers expressed gratitude to the investigator for the interest displayed by the hospital and the health department in her infant. The interview was so constructed that the mother would not suspect the nature of the telephone call, and rigid criteria regarding the presence of purulent material were maintained for classification of a case as positive. Accuracy was checked by an additional feature: in cases where a staphylococcic infection was suspected, the mother was asked to describe the duration and treatment of the illness and to name the physician consulted. In 87% of the cases identified by the telephone survey infants were treated by physicians for their disease. In many cases the physician had told the mother that the baby was suffering from staphylococcic infection.

The telephone survey can be used also to obtain a crude evaluation of measures of epidemic control and measures of disease prevention. Surveillance of a nursery situation can be achieved by spot checks of mothers every three to four months; in this way, insidious staphylococcic problems will not continue unrecognized and uncontrolled.

The investigation revealed that although a large number (some 42%) of infants infected by the "epidemic" strain developed suppurative infection, nasal infection was not the only factor which predisposed the infant to clinical disease. Whereas, during an eight and one-half–month period from mid-December, 1957, through August, 1958, roughly corresponding to the epidemic period, only 6.2% of the infants were found to harbor staphylococci of type 80/81 on the basis of a single nasal discharge culture, the rate of attack among infants during this same period was 21.7%. The fact that 42% of the babies harboring phage type 80/81 in their noses developed suppurative disease, in contrast to the 11.1% of infants harboring other strains who developed disease, confirms the virulent nature of this "epidemic" strain of staphylococcus and its propensity to cause neonatal infection. Jellard[16] suggested that the stump of the umbilical cord is a reservoir of infection in nurseries and showed that the population of staphylococci can be reduced by treatment of the umbilical area with triple dye (brilliant green 2.3 grains [138 mg.], proflavine hemisulfate 1.1 grains [66 mg.], gentian violet 2.3 grains [138 mg.], water 1,000 ml.).

No evidence was encountered to suggest that spread of infection occurred from mother to infant. The rate of attack in mothers was quite low when compared with that in newborn infants, and comparison of staphylococci carried by mothers and their infants did not reveal any similarities. Moreover, the fact that 93% of maternal infections occurred after discharge, with a median interval of 25.5 days from delivery to onset of infection, suggested that the infant was probably the vector of infection for the mother. In most cases in which the mother became infected the infant had already developed a staphylococcic infection.

Indirect evidence was obtained to suggest that two sources of staphylococcic infection existed for the babies. Fourteen per cent of the personnel maintaining working contact with the maternity-nursery unit were found to be nasal carriers of phage type 80/81. When these carriers were removed from the nursery in January, 1958, a decrease in infection occurred, probably reflecting a reduction in the reservoir of this organism in the nursery (fig. 1). However, adequate control of the outbreak was not achieved until the institution of compulsory rooming-in of infants, in late July, 1958. The establishment of rooming-in appears to have succeeded in breaking the chain of transmission of infection from infant to infant.

Immediately after delivery the infant was weighed in the delivery room by the nurse. The baby was then removed to a bassinet, adjacent to the bed of the mother. Demonstration of infant care was given to the mother by a nurse, and from then on the mother was expected to assume full responsibility for the care of her baby. If the mother was unable to care for her baby because of complications, the nurse assumed responsibility. The husband, who was the only visitor allowed in the unit, put on a cap, mask, and gown before entering. All examinations by the physician were performed in the bassinet, at the bedside of the mother. Infants were not removed from the mothers' rooms until discharge from the hospital, except for circumcision. The aim of rooming-in in this particular situation was to minimize contact of the newborn infant with anyone except his mother.

The number of infections declined significantly subsequent to the institution of rooming-in and has remained low for six months. Comparison of rates of attack before and after rooming-in are impressive: 37.5% of infants were infected before the establishment of this control, contrasted with 5.0% since that time. Likewise, the rates of attack for maternal infection have decreased from 5.1 to 1.4%.

This study suggests that rooming-in, presumably by minimizing infant-to-infant contact, was the single most effective control measure in the termination of this epidemic.

Summary

In an outbreak of staphylococcic infections among newborn infants and mothers at a small community hospital case-finding of infections was achieved by three methods, but principally by a telephone survey of mothers six weeks after delivery. The telephone survey was found to be a rapid, efficient, and accurate case-finding technique.

Sixty-five per cent of staphylococci cultured from lesions were of phage type 80/81. The rate of infection during a 16-month surveillance period was 25.6% among newborn infants and 3.7% among mothers. The number of deliveries associated with infections was 37.1% during the epidemic period and 6.8% during the nonepidemic period. Infant pyoderma was the disease most commonly manifested. Of the infant lesions 65.9% occurred after discharge from the hospital; of the maternal lesions 93.3% occurred after discharge.

Among the measures employed to control the epidemic of staphylococcic infections were removal of hospital personnel who were nasal carriers of the 80/81 strain from the nursery, improvement of aseptic techniques, discharge of infants and mothers three days after delivery, and compulsory rooming-in of the infant with the mother. It is concluded that rooming-in was the single most important step in the termination of the outbreak.

Peter Bent Brigham Hospital, Boston 15 (Dr. Farrer).

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LIFE OUTSIDE THE BODY.—Some tissue cells adapt or alter to "in vitro" conditions when cultivated for prolonged periods by the tissue culture technique. This adaptation to form cell strains is manifest by a change to a uniform morphology, by a marked increase in the rate of cell proliferation, and by the ease with which trypsinized cultures attach to the glass culture flask.—R. V. Andrews, H. J. Phillips, and V. Skank, Metabolism of Normal and Malignant Tissue Culture Cell Strains, *The Physiologist,* August, 1959.

EPIDEMIOLOGY OF STAPHYLOCOCCIC INFECTION IN NURSERY OF SMALL COMMUNITY HOSPITAL

Beatrice Kresky, M.D.
and
Herbert L. Elias, M.D., Rockville Centre, N. Y.

It is easier to prevent a nursery outbreak of staphylococcic infection than to bring under control a full-blown epidemic. A 10-part program aimed at controlling an epidemic is detailed, the main points being isolation of all infected infants and those with positive cultures, administration of an antibiotic to all newborn infants, and temporarily excusing from duty all nursing personnel harboring staphylococci in the nasopharynx. Staphylococcic infection is frequently endemic in the community among neonatal infants and postpartum women before it becomes epidemic in a nursery. Cases developing at home are greater in number and clinically more severe than the nursery cases. Information about community dissemination may be obtained by a questionnaire sent to the mother when an infant is 2 months old.

In recent years attention has been focused on the increasing incidence of staphylococcic infection in hospital patients. These infections have occurred most frequently among groups peculiarly susceptible, such as newborn infants, persons debilitated from chronic disease, and surgical patients.

It has been shown that in a nursery outbreak of staphylococcic infection the majority of infected infants and carriers harbor strains of Staphylococcus aureus, coagulase-positive, which are identical in respect to phage type and antibiotic sensitivity.[1] The most common phage type isolated from nursery cases is known as type 80/81, which includes mutations of type 42 B, 44 A, 52, and 47 C.[2] Many nursery outbreaks of staphylococcic infection caused by these strains have occurred in the United States, England, and Australia.[1] This strain is usually resistant to penicillin, the tetracyclines, and streptomycin but sensitive to erythromycin, chloramphenicol (Chloromycetin), nitrofurantoin (Furadantin), and novobiocin, although the antibiotic sensitivity of a phage type may change at any time.[3]

It is generally accepted that in a hospital nursery infection is transmitted from baby to baby and from carriers harboring the epidemic strain to baby, but not from mother to baby, although an infected infant can transmit infection to the nursing mother.[4] The carrier rate of staphylococci in healthy infants in a hospital nursery is zero at birth but may be as high as 40% by the 4th day of hospital life, and as high as 80% by the 8th day.[5] Only 8% of infants born at home or in a hospital with a rooming-in system have positive cultures on the 8th day of life.[6]

Eichenwald[7] believes that some babies, known as "cloud babies" and infected by staphylococci in the first days of life, disseminate the organism into the atmosphere. Staphylococci can be cultured consistently from their bed linen, bassinets, and the surrounding air. Other observers have reported that infant-to-infant colonization occurs through air transmission and by means of fomites rather than human carriers. Wysham[8] reported that in one epidemic the nurses and attendants harbored a strain of staphylococcus differing from that of the infants. However, the infectious strain could be cultured from the air, dust, and linen in the nursery.

A reservoir of infection frequently exists in the nose and throat of hospital personnel. Several nursery epidemics have been traced to carriers among nursery attendants.[9]

All extremes of staphylococcic infection have occurred in the neonatal period, ranging from self-limited impetigo to septicemia, osteomyelitis, and staphylococcic pneumonia. Certain infants develop pyoderma while in the nursery, but a greater number are discharged well and develop clinical disease from 2 to 12 weeks after leaving the hospital.[10]

Clinical disease among mothers is rare in the obstetric unit, but furunculosis, mastitis, and breast abscess frequently occur at home, after discharge from a hospital where a focus of staphylococcic infection exists.[11] Cases of pyoderma are reported among siblings of infants infected by staphylococci while in the nursery.[3] The magnitude and ramifications of an outbreak having its source in the nursery cannot be accurately assessed unless a survey is made of the community served by the hospital.

South Nassau Communities Hospital is a 250-bed hospital in the southern section of Long Island, N. Y., serving a population of approximately 300,000. The obstetric service accommodates 48 newborn infants and 40 mothers. The census of live births varies from 20 to 25 in any one day. In the period from Jan. 1 to July 31, 1958, 1,033 live infants were delivered at South Nassau Hospital. The nursery personnel consists of 47 permanent nurses and 27 relief nurses and nurses' aides. The technique fol-

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From the South Nassau Communities Hospital, Oceanside, N. Y.

lowed in the nursery is essentially that advocated in the manual on the hospital care of newborn infants of the American Academy of Pediatrics.[12]

In the period from Jan. 1 through July 31, 1958, there were 28 cases of staphylococcic infection in the maternity service: one mother and 27 infants (fig. 1). In addition, from Jan. 1 through July 31, 1958, 36 cases of staphylococcic infection occurred in mothers and infants at home, after discharge from the maternity service: 8 in mothers and 28 in infants (fig. 2). The medical staff were not cognizant of these home cases until a retrospective survey of the community was made several months after the nursery outbreak. The number of home and hospital cases totaled 64, an infection rate of 6% of the total number of live infants (fig. 3).

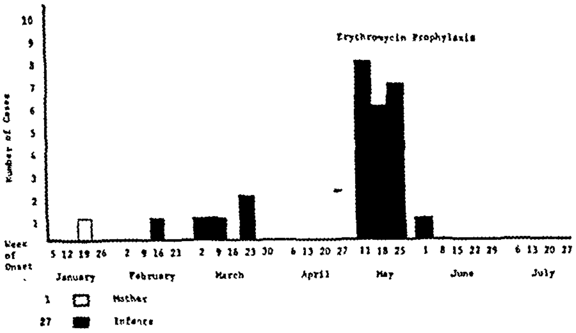

Fig. 1.—Incidence of staphylococcic infections in nursery for newborn infants in South Nassau Communities Hospital.

Nursery Outbreak

On Jan. 5, 1958, a mother developed an infection in an episiotomy wound from which staphylococci were cultured. Seventeen days later an infant, who had been discharged well, was readmitted to the pediatric service, with a staphylococcic abscess of the breast. A week later a second infant was readmitted, with cellulitis of the back from which staphylococci were isolated. The following week, an infant with cellulitis of the face was seen at home by one of us. The next week, a mother who had delivered at South Nassau Hospital was readmitted to the surgical service with a breast abscess. It is interesting, yet at the same time discouraging, to note that no effort was made to link these cases to a focus in the nursery. During this six-week period, five cases of pyoderma occurred in infants in the nursery, each separated by about one week, with no two cases occurring on the same day.

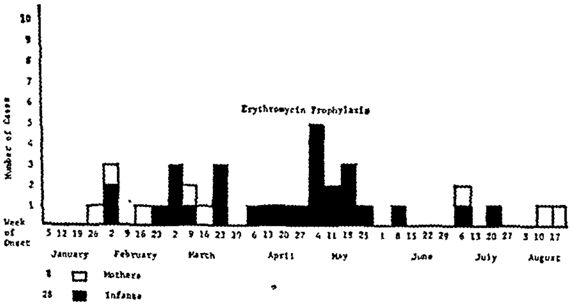

Fig. 2.—Incidence of staphylococcic infection after discharge from obstetric unit of South Nassau Communities Hospital.

No further cases of staphylococcic infection developed until five weeks later, when the first death occurred during the last week in April. An infant, discharged from the nursery apparently well, was found dead at home one week after discharge. Autopsy revealed staphylococcic pneumonia and empyema. On May 9, an infant was readmitted to the pediatric service with sepsis, subsequent to an attack of cellulitis of the scalp. This infant died and blood culture revealed staphylococci.

On the same day a second infant born at South Nassau Hospital was readmitted with an overwhelming septicemia. He died the day of admission. Autopsy revealed septicemia due to Escherichia coli, with kidney abscesses. However, staphylococci with the same antibiotic sensitivity as that of those in the infant who died of staphylococcic septicemia were cultured from the nose and throat. Prior to the onset of the septicemia, the infant had had a pustular rash over the lower part of the abdomen. It was discovered that the mothers of both infants dying of septicemia had shared a room in the maternity service. This third death may be considered a primary staphylococcic infection, with an overwhelming secondary septicemia due to Esch. coli.

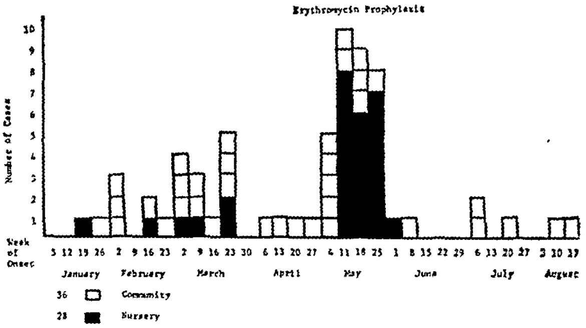

Fig. 3.—Incidence of staphylococcic infection in nursery for newborn infants in South Nassau Communities Hospital and in surrounding community.

During the week of May 11 there was a sudden sharp increase in the cases of pyoderma in the nursery; eight cases the week of May 11, six cases the week of May 18, and seven cases the week of May 25 (fig. 1).

Attempts at controlling the spread of infection in the nursery were begun on May 14. Well babies were isolated from infected babies. Mothers of babies with positive nose and throat cultures or clinical infection were separated from mothers of well babies. So-called contaminated nurseries were temporarily closed, washed, painted, and then re-

PREMEDICATION—AN OLD IDEA AND NEW DRUGS

John Adriani, M.D., New Orleans

Drugs to be used as premedicants before general or local anesthesia is induced must be selected with due regard to the patient's physical and mental state, the major anesthetic to be used, and the technique of administration. They should be prescribed by the person assigned to administer the anesthetic. Their purpose is to relieve the patient's anxiety, to reduce the amount of troublesome mucous secretions, to intensify the desired effect or reduce the required amount of the major anesthetic, and to decrease the incidence of complications of anesthesia, such as cardiac arrest, laryngospasm, and bronchial spasm. It is doubtful whether any of the drugs recently introduced for these purposes are preferable to the customary combination of a narcotic and a belladonna alkaloid.

The custom of prescribing sedatives to be given an appreciable time before the principal anesthetic is administered is nearly as old as the practice of anesthesia itself. Primarily, the purpose of such premedication is to obtain psychic sedation so that the patient is tranquil, nonanxious, and indifferent when he arrives in the operating room. Besides obtaining psychic sedation, however, there are at least three other purposes for premedication: It is given to minimize secretion of mucus in the respiratory tract, to offset the undesirable side-effects of some anesthetics, and to fortify impotent anesthetics.

Basic Concepts

The basic concepts of premedication have changed little since the idea was conceived. The techniques, however, are being varied and modified as new anesthetics and premedication agents are introduced. The trend toward the use of combinations of drugs instead of a single-principle anesthetic has been responsible for the departure from standard practice. In addition, better drugs are being sought, since no agent has been found which is ideal and wholly free from side-effects.

Premedication, to use the words of Claude Bernard, as cited by Duncum,[1] is mixed anesthesia. As such it is part of the anesthetic. Therefore, it should be prescribed by the person assigned to administer the anesthetic. The selection is made on the basis of the general status and the psychic make-up of the patient and the type and technique of anesthesia to be employed. Too often the selection is left to the discretion of persons who are not directly concerned with the administration of the anesthetic and who are unaware of what has been planned for the patient from that standpoint.

Sedation and tranquillity may be obtained by use of one or several of a host of central-nervous-system depressants. Claude Bernard was instrumental in the adoption of morphine as a premedicant.[1] Since that time the use of narcotics has been widely accepted. Several years later, according to Duncum, Forné and others used chloral hydrate for basal anesthesia. Deep hypnosis was produced on which was superimposed inhalation anesthesia with chloroform. The [illegible]s of "light" or "heavy" premedication had [illegible]eginnings at this time and [illegible]t-day practice. [illegible]d of anesthesia soon [illegible] combined [illegible] that scopolamine enhanced them. These facts, known for so long, are not fully appreciated. The combination of atropine and morphine is still widely used. Scopolamine combined with the narcotic has a tranquilizing and amnesic action not possessed by morphine alone.

Newer Drugs

As each hypnotic or narcotic has been introduced it has been evaluated as a premedicant. The morphine used by Claude Bernard and the chloral hydrate of Forné were the prototypes of the numerous drugs which have since been used for premedication. A host of drugs have been used whose effects vary from the mild sedation produced by phenobarbital to the deep hypnosis produced by rectally given tribromoethanol (Avertin), intravenously given thiopental and hydroxydione, and similar potent basal narcotics. The types of compounds range from simple aliphatic alcohols to ones with complex heterocyclic molecular structures. The anesthetist is thus permitted a latitude from light sedation to deep narcosis, depending on personal preference and the expediency of the situation. The more profound the sedation, the greater the physiological disturbance which one must anticipate.

The most recent trend in premedication centers [illegible]ut use of the ataraxics. The narcotics and hyp[illegible]ly on the cortex and depress from [illegible]. The ataraxics behave differently. [illegible]ly on the subcortical [illegible] the control of the emo[illegible] [illegible]cate emotionally disturbed patients has been well established. That they do the same to "normal" patients is less certain. Scopolamine was the only drug manifesting a subcortical action that was used with the narcotics prior to the introduction of tranquilizers. The number of drugs being offered in the latter group is large and is rapidly increasing. To be considered modern, it appears one must cast aside the old and take on the new. As each new depressant with sedative properties is introduced it is offered to anesthetists as a possible premedicant. As a result, a wave of enthusiastic reports is appearing which describe the use of drugs which have been superficially studied and which contain conclusions drawn from clinical impressions and not from controlled well-planned studies.

Value of Narcotics

Some anesthetists have expressed disapproval of narcotics for premedication.[2] Objections offered are that these drugs depress respiration; cause hypotension, nausea, and vomiting; increase postoperative morbidity; and cause other untoward effects. One commonly voiced objection is that patients scheduled for an elective operation are not in pain and, therefore, do not require a narcotic. The sedation provided by short-acting barbiturates, such as pentobarbital or secobarbital in orally given doses of 100 mg., is recommended as being as efficacious. The opponents of the narcotics have been quite vociferous and have created much confusion concerning the pros and cons of their use.

Should the narcotics be cast aside? Are the objections which are voiced based on fact or prejudice? The narcotics have been used (with good results and without ill-effects) in too many patients, for too long a time, by too many anesthetists to be casually cast aside on the basis of untoward responses in isolated cases, evidence from studies on small series of patients, or the behavior of volunteers subjected to tilting. The argument that the patients undergoing elective surgery are not in pain and, therefore, do not require a narcotic is superfluous. Narcotics are not administered preoperatively for their pain-relieving qualities. Narcotics, it is true, elevate the pain threshold. However, this elevation is effective up to a given point of dosage, beyond which little additional relief is obtained.

Much of the beneficial effect of a narcotic, however, is accomplished by the alteration of the psychological response to pain.[3] In other words, the patient continues to experience the pain but becomes indifferent to it. A habitué craves a particular drug not because he is in pain but because he derives a sense of well-being from it. In other words, narcotics relieve anxiety. It is for this reason that they are used for premedication. The barbiturates and other central-nervous-system depressants do not accomplish this end as effectively because their mechanism of action is different. They are, relatively speaking, less potent. Whatever sedation they do cause is mild if they are administered in hypnotic doses. Doses which produce a state of basal narcosis are necessary to render the patient amnesic and indifferent to his environment. Doses required to obtain this effect have most, if not all, of the drawbacks of the narcotics. Generally, the hypnotic dose of secobarbital or pentobarbital is inadequate and is fortified with intravenously given thiopental when the patient arrives in the operating room. When narcotics are used, this additional fortification of the sedation with a potent basal narcotic is not necessary.

The ability to cause hypotension and respiratory depression is an attribute of all central-nervous-system depressants and is not peculiar to the narcotics. It is common to find that, when one central-nervous-system depressant causes difficulty in a particular patient, others produce the same type of response, if used in quantities to produce similar degrees of depression. To single out narcotics among the group of central-nervous-system depressants as being objectionable in this regard is not correct. One alleged advantage the narcotics have over other sedatives is that untoward reactions are easily recognized and treated. Antagonists such as nalorphine (Nalline) and levallorphan (Lorfan) are available in the event such effects are encountered. Use of these is seldom necessary, however, when narcotics are used judiciously.

Any justification of the opposition to narcotics stems from experiences caused by their misuse rather than their widespread use. The routine use of narcotics without individualization obviously leads to difficulty, as will such use of any drug. Most difficulties have arisen when narcotics have been used in patients who should not have had them, when they have been used to excess to the point of inducing unconsciousness, or when they have been used and could have been omitted. Such misuse leads to the much complained of severe respiratory depression and hypotension. A common error is to administer the doses of narcotic ordinarily required for robust young patients to elderly patients. Elderly patients have less tolerance to central-nervous-system depressants than young or middle-aged persons. It is customary to reduce the dose of a narcotic to one-half, one-fourth, or even one-sixth of that required for middle-aged patients.

Most anesthetists obtain excellent sedation with use of a combination of morphine and scopolamine. Ten milligrams of morphine combined with 0.4 mg. of scopolamine administered subcutaneously one and one-half hours prior to anesthesia in an average adult produces tranquillity, an air of indifference, and amnesia without circulatory and respiratory depression. Consciousness is not lost, and the patient is able to converse, is aware of his environment, is relaxed, and is not anxious. The scopolamine enhances the cortical effects of morphine. As is the case with atropine, scopolamine appears to antagonize the depressant effect of morphine on the medullary centers.

opened. Nose and throat cultures were taken from all nursing personnel. Nurses harboring staphylococci were restricted to caring for infants with pyoderma and/or with postive nose and throat cultures. Washing with hexachlorophene soap was substituted for dry skin care. Despite these measures, a sharp increase in the number of nursery cases occurred, as shown in figure 1.

On May 26, 1958, the following procedures recommended for the control of staphylococcic infection were instituted [13]: 1. Infants with pyoderma and infants harboring staphylococci without clinical disease were isolated in one unit. Mothers of these infants were separated from newly delivered mothers. 2. All newborn infants and their mothers were admitted to an uncontaminated unit and had no contact with the group described above. 3. There was no interchange of nursing care. Mothers and infants in each group were cared for by separate nurses. 4. All infants after 12 hours of age received 44 mg. of erythromycin per pound per day for five to six days. 5. All infants were bathed initially with hexachlorophene soap and water, and daily skin care was continued with 1:1,000 aqueous benzalkonium (Zephiran) chloride solution. 6. Infants were discharged on the third hospital day. 7. Performance of circumcisions was discontinued. 8. Weekly nose and throat cultures were taken from all personnel in the delivery room, in the maternity unit, and in the nursery. 9. Nurses with positive nose and throat cultures received 1 Gm. of erythromycin per day in divided dosage for four days, and remained off duty, at home, with pay, until two successive negative nose and throat cultures were obtained 24 hours apart.

TABLE 1.–*Antibiotic Sensitivity of Staphylococci Cultured from Patients with Infection and Carriers During Epidemic in South Nassau Communities Hospital*

	Positive Cultures	Antibiotic Sensitivity	Identical Antibiotic Sensitivity
Nurses	64	7	6
Infants in nursery	20	6	5
Infants and mothers rehospitalized	10	6	5
Total	94	19	16(84%)
Patients other than mothers and infants	17	14	2

Within one week of institution of the above control measures, the number of cases in the nursery decreased sharply (fig. 1). The number of home cases also declined immediately (fig. 2).

A comparison of figures 1 and 2 shows that 24 (69%) of the home cases occurred prior to the explosive outbreak in the nursery. The staphylococcic infection in the neonatal period appears to be endemic in the community before it becomes overtly epidemic in the nursery. The incidence of home cases remained relatively constant until July 1. Within one week of the prophylactic administration of erythromycin to the nursery infants, the number of home cases declined sharply.

The taking of weekly nose and throat cultures was begun on nurses and attendants in the obstetric unit early in May, when it was realized that an epidemic situation existed. At the height of the nursery outbreak staphylococci could be isolated from the noses and throats of 45% of the nurses. The organisms was isolated from only 25% of the staff of the delivery room, where relief nurses were not employed.

Antibiotic sensitivity studies were done on organisms isolated from infants in the nursery, carriers among the nursery staff, and home cases of patients readmitted to the hospital. Eighty-four per cent exhibited identical antibiotic sensitivities (table 1). The organism was resistant to penicillin, sulfisoxazole (Gantrisin), and streptomycin, and sensitive to the tetracyclines, chloramphenicol, nitrofurantoin, aureomycin, erythromycin, and novobiocin. This is presumptive evidence that the nursery outbreak and its community ramifications were caused by an identical strain of staphylococcus.

From January through July, 1958, 17 patients, other than mothers and infants born at South Nassau Hospital, were admitted to the hospital with staphylococcic infections. Fifteen had widely varying antibiotic sensitivity patterns, and two had similar patterns. None was identical to the antibiotic sensitivity pattern exhibited by mothers, infants, and nurses involved in the nursery outbreak (table 1).

Community Survey

It became apparent from the number of hospital readmissions that ramifications of the nursery outbreak must have existed in the community. In September, 1958, a questionnaire was mailed to 75 physicians who had performed deliveries at South Nassau Hospital from January through July, 1958, inquiring about the number and type of infections in mothers and infants under their care. Seventy of the 75 physicians replied.

Physicians reporting cases of infection were telephoned, and clinical and laboratory information was obtained. Wherever possible, records of hospitalization were checked. It was found that 28 infants and 8 mothers had some form of staphylococcic infection severe enough to warrant medical care (fig. 2). Table 2 shows the type of clinical disease in these patients. Three infants died, two from septicemia and one from staphylococcic pneumonia and empyema.

The cases occurring at home were clinically more severe than those occurring in the nursery. All of the nursery infants were given diagnoses of pyoderma without complications or sequelae.

Mothers probably developed staphylococcic infection at home from babies infected in the hospital. Only one infant of the eight infected mothers had clinical disease. The three mothers with breast abscess had nursed their babies.

Comment

Investigation and control of an outbreak of staphylococcic infection is a new concept in preventive medicine. Our understanding is incomplete with respect to endemic and epidemic manifestations of the disease, changing virulence of the organism, and the role of nasal carriers, fomites, and air in the transmission of infection.

Wentworth and co-workers[3] sum up the problems inherent in the investigation of a nursery outbreak of staphylococcic infection as follows: "a hospital administrative staff unaware of the extent of the ramifications of the situation, a frightened nursery staff liberally seeded with feelings of guilt concerning their role in the epidemic and faced with grossly inadequate laboratory facilities for surveillance of the situation."

The first principle derived from the study of the outbreak at the South Nassau Communities Hospital is the importance of correct assessment of the situation by the hospital staff and by physicians in the community. Staphylococcic infection has an insidious onset and is usually endemic in the community before it becomes overtly epidemic in the nursery. The presence of one or two cases of pyoderma in a nursery cannot be ignored and warrants investigation of isolation techniques, carrier rates, and the number of staphylococcic infections in the community served by the hospital. Hardyment[14] feels that the incidence of pyoderma and conjunctivitis in a nursery during a nonepidemic period should be less than 1%.

The outbreak at South Nassau Hospital probably originated in January, with a mother who had an infected episiotomy wound from which staphylococci were cultured. The readmission to the hospital of infants and mothers with staphylococcic infection, the few cases of pyoderma in the nursery, and the gradual seeding of the community with staphylococci were not linked together until the three deaths occurred, three months after the initial case.

The outbreak found the hospital unprepared in terms of laboratory facilities. At the onset of the epidemic, because of socioeconomic pressures, difficulty in rapidly replacing nursing personnel, and varying opinions as to whether or not carriers should be isolated, nurses with positive cultures were not removed from duty. Thus the medical staff probably increased the dissemination of infection throughout the nursery inadvertently. There was no centralized community agency to which one could turn for assistance in recommending control procedures, investigation of the incidence of home cases, and provision of laboratory facilities for isolation, antibiotic sensitivity tests, and phage-typing of the organism.

A nursery outbreak has an insidious onset. For a few months there may be only one or two cases of pyoderma or conjunctivitis in the nursery. However, newborn infants are constantly being infected by staphylococci through infant-to-infant transmission, by air, dust, and fomites and by nursery personnel harboring the organism. As the number of infected infants increases, the number of attendants harboring the "nursery strain" of staphylococci increases. Eventually this culminates in an explosive nursery outbreak of pyoderma and furunculosis.

Due to the discharge of well infants infected by staphylococci, community dissemination occurs at a rapid rate before an explosive nursery outbreak. Cases of pyoderma, mastitis, cellulitis, pneumonia, and septicemia occur in infants at home. Infants harboring staphylococci transmit infection to mothers, and cases of furunculosis, mastitis, and breast abscess occur. Siblings may contract staphylococcic infection from the infected infants.

Table 2.—*Clinical Diagnosis in Thirty-six Cases of Staphylococcic Infection Occurring After Discharge from Obstetric Unit*

Diagnosis	Infants	Mothers
Pyoderma	9	2
Cellulitis	8	0
Mastitis and breast abscess	8	3
Septicemia	2	0
Pneumonia	1	0
Perineal abscess	0	2
Parametritis	0	1
Total	28	8

The home cases appear to be clinically more severe than the nursery cases. Perhaps the longer incubation period of the home cases steps up the virulence of the organism. Perhaps infant resistance to staphylococci decreases at the end of the neonatal period because of the low level of gamma globulin in the blood at this time.[15] Opsonins against staphylococci in the blood of infants are at adult levels at birth, decrease for the first two months of life, and then rise again to adult levels.[16]

An increase in staphylococcic infection in the community served by a hospital is a danger signal that trouble is brewing in the nursery and calls for immediate investigation. There are several ways of keeping track of staphylococcic infection in the community: 1. Infections in infants during the neonatal period and in postpartum women should be made reportable to the local health department. 2. Mothers should return a questionnaire to the hospital when the infant is 2 months old. The form can be couched in terms which would avoid suspicion of the hospital as a focus of infection and appear merely to express interest in the welfare of the infant (table 3). 3. Physicians should report to the hospital of delivery on the incidence of infection in infants and mothers under their care (table 4). Data obtained from the above sources should be reviewed at regular intervals by the "infection committee" of the hospital.

TABLE 3.—*Sample of Questionnaire Addressed to Mothers of Two-Month-Old Infants to Ascertain Incidence of Staphylococcic Infection*

Name: .... Date of Birth:...........
Weight at one month of age: ....
Did you nurse your baby? ....
Has he been sick? ....
  If so, what illness? ....
  Was a physician consulted? ....
Has he had any skin rashes? ....
  Describe: ....
Has he had any eye infections? ....
  Describe: ....
Has any other member of your family been ill? ....
  If so, relation: ....
    What Illness? ....
Have you been ill? ....
  If so, what illness? ....

Controversy exists in the literature concerning procedures for control of a nursery epidemic of staphylococcic infection. Certain groups believe that an antibiotic to which the particular strain is sensitive should be administered prophylactically to all newborn infants in a "contaminated" nursery and to all attendants harboring staphylococci.[17] Other groups believe that antibiotic prophylaxis not only is unnecessary but may prove harmful, as staphylococcus is an organism which rapidly develops antibiotic resistance.[4]

It is our experience that auxiliary measures such as isolation of infected infants, change from dry skin care to wet skin care, use of hexachlorophene soap and benzalkonium chloride solution, shortening of the hospital stay, closing of contaminated nurseries, and the reopening of them after washing and painting did not stop the spread of staphylococci. Administration of erythromycin to all newborn infants from the 1st to the 10th day of life brought the nursery outbreak to an immediate halt and checked the community dissemination of staphylococci. Administration of erythromycin to all nurses with positive cultures, and their removal from duty until two successive negative nose and throat cultures had been obtained, was instrumental in stopping the spread of staphylococci.

It is easier to prevent a nursery outbreak than to bring under control a full-blown epidemic. Measures which may be ineffective in stopping an outbreak will prove successful in preventing staphylococcic infections from gaining a foothold. Generally recommended procedures are as follows [18]:

1. Routine bimonthly nose and throat cultures of attendants and nurses. Isolated organisms should be phage-typed and tested for antibiotic sensitivity. An increase in the percentage of persons with positive nose and throat cultures is a signal for immediate epidemiologic and technical investigation of the nursery.

2. Nose and throat cultures should be taken from newborn infants at bimonthly intervals. Phage-typing should be done on all organisms isolated for antibiotic sensitivities. A sudden increase in the number of infants harboring staphylococci calls for investigation of the nursery.

3. Nursery procedures and techniques of infant care should be regularly reviewed by the "infection committee" of the hospital and any deficiencies remedied.

4. Cultures of air, dust, linens, nursing bottles, bottle warmers, and other utensils should be obtained at bimonthly intervals.

5. Routine washing of infants with hexachlorophene soap is more efficacious than dry skin care.

6. Infants with pyoderma should be isolated in a separate unit and cared for by an independent nursing staff.

7. Nurses who are chronic carriers of the "nursery strain" of staphylococci should be permanently removed from the obstetric unit.

8. The hospital stay should be shortened to an extent compatible with the health of mother and infant. There is a direct relation in infants between the proportion of positive nose and throat cultures and the length of the nursery stay.[6]

TABLE 4.—*Sample of Physician's Report to Hospital of Delivery on Incidence of Infection in Infants and Mothers*

Name of Family: .... Address: ....
                                                   ....
Infant's Date of Birth: ....
Presence of Infection:
  Infant: ....
  Mother: ....
  Siblings: ....
Diagnosis: .... Course: ....
           ....
Treatment: .... Laboratory: ....
           ....
           ....

9. There should be no interchange of nurses from floor to floor in the hospital, and only minimal employment of relief personnel.

10. Staphylococcic infection in postpartum women and in infants during the neonatal period must be reported to a central agency.

Disagreement in the literature concerning the type and extent of control measures for a nursery outbreak of staphylococcic infection is due chiefly to lack of knowledge concerning virulence factors. Some persons seem to harbor staphylococcus type 80/81 with impunity. Others have recurrent bouts of mild illness, while still others die from severe infection. Attempts have been made to link virulence with change in host resistance. Infants and children may harbor a virulent strain of staphylococcus in the nasopharynx without ill-effects, but when a viral respiratory infection supervenes a synergistic action between the virus and the bacteria may occur and clinical disease may develop.[7]

Staphylococci may be cultured from the skin and umbilicus of many newborn infants who do not have clinical disease. However, the onset of respiratory distress, diarrhea, a break in the skin, circumcision, or a diaper rash may precipitate clinical infection, ranging from pyoderma to septicemia. Neither the carrier state nor active staphylococcic infection causes the development of any immunity to subsequent invasion by the same strain.

Present knowledge of the biochemical properties of the staphylococcus such as phage type, coagulase production, and alpha hemolysin and leukodicin production do not adequately explain virulence factors inherent in the organism. Understanding of the epidemiology of staphylococcic infection will remain incomplete until the problems of pathogenicity and immunity are solved.

Summary

An epidemic outbreak of staphylococcic infection in the nursery of a small community hospital was controlled by (1) complete isolation of all infected infants and infants with positive nose and throat cultures, (2) prophylactic administration of erythromycin to all newborn infants, and (3) the temporary severance from duty, with pay, of all nurses harboring staphylococci in the nasopharynx, until two successive negative nose and throat cultures had been obtained, 24 hours apart.

Staphylococcic infection is frequently endemic in neonatal infants and postpartum women before it becomes epidemic in the nursery. The cases of staphylococcic infection developing at home after the mother's discharge from the obstetric service were greater in number and clinically more severe than the nursery cases. Community dissemination of staphylococcic infection ceased after prophylactic administration of erythromycin to all infants in the nursery.

Suggested procedures for the prevention and control of infection in the nursery and community are that (1) staphylococcic infection in neonatal infants and in postpartum women be made reportable to the local health department and (2) information about community dissemination be obtained by a questionnaire sent to the mother when an infant is 2 months old.

61 Hempstead Ave. (Dr. Kresky).

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PREMEDICATION—AN OLD IDEA AND NEW DRUGS

John Adriani, M.D., New Orleans

Drugs to be used as premedicants before general or local anesthesia is induced must be selected with due regard to the patient's physical and mental state, the major anesthetic to be used, and the technique of administration. They should be prescribed by the person assigned to administer the anesthetic. Their purpose is to relieve the patient's anxiety, to reduce the amount of troublesome mucous secretions, to intensify the desired effect or reduce the required amount of the major anesthetic, and to decrease the incidence of complications of anesthesia, such as cardiac arrest, laryngospasm, and bronchial spasm. It is doubtful whether any of the drugs recently introduced for these purposes are preferable to the customary combination of a narcotic and a belladonna alkaloid.

The custom of prescribing sedatives to be given an appreciable time before the principal anesthetic is administered is nearly as old as the practice of anesthesia itself. Primarily, the purpose of such premedication is to obtain psychic sedation so that the patient is tranquil, nonanxious, and indifferent when he arrives in the operating room. Besides obtaining psychic sedation, however, there are at least three other purposes for premedication: It is given to minimize secretion of mucus in the respiratory tract, to offset the undesirable side-effects of some anesthetics, and to fortify impotent anesthetics.

Basic Concepts

The basic concepts of premedication have changed little since the idea was conceived. The techniques, however, are being varied and modified as new anesthetics and premedication agents are introduced. The trend toward the use of combinations of drugs instead of a single-principle anesthetic has been responsible for the departure from standard practice. In addition, better drugs are being sought, since no agent has been found which is ideal and wholly free from side-effects.

Premedication, to use the words of Claude Bernard, as cited by Duncum,[1] is mixed anesthesia. As such it is part of the anesthetic. Therefore, it should be prescribed by the person assigned to administer the anesthetic. The selection is made on the basis of the general status and the psychic make-up of the patient and the type and technique of anesthesia to be employed. Too often the selection is left to the discretion of persons who are not directly concerned with the administration of the anesthetic and who are unaware of what has been planned for the patient from that standpoint.

Sedation and tranquillity may be obtained by use of one or several of a host of central-nervous-system depressants. Claude Bernard was instrumental in the adoption of morphine as a premedicant.[1] Since that time the use of narcotics has been widely accepted. Several years later, according to Duncum, Forné and others used chloral hydrate for basal anesthesia. Deep hypnosis was produced on which was superimposed inhalation anesthesia with chloroform. The customs of "light" or "heavy" premedication had their beginnings at this time and have continued into present-day practice.

The early workers in the field of anesthesia soon learned that atropine and scopolamine combined with morphine suppressed salivation and secretion of mucus.[1] They also commented that atropine appeared to antagonize the effects of morphine and that scopolamine enhanced them. These facts, known for so long, are not fully appreciated. The combination of atropine and morphine is still widely used. Scopolamine combined with the narcotic has a tranquilizing and amnesic action not possessed by morphine alone.

Newer Drugs

As each hypnotic or narcotic has been introduced it has been evaluated as a premedicant. The morphine used by Claude Bernard and the chloral hydrate of Forné were the prototypes of the numerous drugs which have since been used for premedication. A host of drugs have been used whose effects vary from the mild sedation produced by phenobarbital to the deep hypnosis produced by rectally given tribromoethanol (Avertin), intravenously given thiopental and hydroxydione, and similar potent basal narcotics. The types of compounds range from simple aliphatic alcohols to ones with complex heterocyclic molecular structures. The anesthetist is thus permitted a latitude from light sedation to deep narcosis, depending on personal preference and the expediency of the situation. The more profound the sedation, the greater the physiological disturbance which one must anticipate.

The most recent trend in premedication centers about use of the ataraxics. The narcotics and hypnotics act primarily on the cortex and depress from above downward. The ataraxics behave differently. They appear to act primarily on the subcortical structures concerned with the control of the emotions. The fact that the ataraxics placate emotion-

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Chairman's address, read before the Section on Anesthesiology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959.

ally disturbed patients has been well established. That they do the same to "normal" patients is less certain. Scopolamine was the only drug manifesting a subcortical action that was used with the narcotics prior to the introduction of tranquilizers. The number of drugs being offered in the latter group is large and is rapidly increasing. To be considered modern, it appears one must cast aside the old and take on the new. As each new depressant with sedative properties is introduced it is offered to anesthetists as a possible premedicant. As a result, a wave of enthusiastic reports is appearing which describe the use of drugs which have been superficially studied and which contain conclusions drawn from clinical impressions and not from controlled well-planned studies.

Value of Narcotics

Some anesthetists have expressed disapproval of narcotics for premedication.[2] Objections offered are that these drugs depress respiration; cause hypotension, nausea, and vomiting; increase postoperative morbidity; and cause other untoward effects. One commonly voiced objection is that patients scheduled for an elective operation are not in pain and, therefore, do not require a narcotic. The sedation provided by short-acting barbiturates, such as pentobarbital or secobarbital in orally given doses of 100 mg., is recommended as being as efficacious. The opponents of the narcotics have been quite vociferous and have created much confusion concerning the pros and cons of their use.

Should the narcotics be cast aside? Are the objections which are voiced based on fact or prejudice? The narcotics have been used (with good results and without ill-effects) in too many patients, for too long a time, by too many anesthetists to be casually cast aside on the basis of untoward responses in isolated cases, evidence from studies on small series of patients, or the behavior of volunteers subjected to tilting. The argument that the patients undergoing elective surgery are not in pain and, therefore, do not require a narcotic is superfluous. Narcotics are not administered preoperatively for their pain-relieving qualities. Narcotics, it is true, elevate the pain threshold. However, this elevation is effective up to a given point of dosage, beyond which little additional relief is obtained.

Much of the beneficial effect of a narcotic, however, is accomplished by the alteration of the psychological response to pain.[3] In other words, the patient continues to experience the pain but becomes indifferent to it. A habitué craves a particular drug not because he is in pain but because he derives a sense of well-being from it. In other words, narcotics relieve anxiety. It is for this reason that they are used for premedication. The barbiturates and other central-nervous-system depressants do not accomplish this end as effectively because their mechanism of action is different. They are, relatively speaking, less potent. Whatever sedation they do cause is mild if they are administered in hypnotic doses. Doses which produce a state of basal narcosis are necessary to render the patient amnesic and indifferent to his environment. Doses required to obtain this effect have most, if not all, of the drawbacks of the narcotics. Generally, the hypnotic dose of secobarbital or pentobarbital is inadequate and is fortified with intravenously given thiopental when the patient arrives in the operating room. When narcotics are used, this additional fortification of the sedation with a potent basal narcotic is not necessary.

The ability to cause hypotension and respiratory depression is an attribute of all central-nervous-system depressants and is not peculiar to the narcotics. It is common to find that, when one central-nervous-system depressant causes difficulty in a particular patient, others produce the same type of response, if used in quantities to produce similar degrees of depression. To single out narcotics among the group of central-nervous-system depressants as being objectionable in this regard is not correct. One alleged advantage the narcotics have over other sedatives is that untoward reactions are easily recognized and treated. Antagonists such as nalorphine (Nalline) and levallorphan (Lorfan) are available in the event such effects are encountered. Use of these is seldom necessary, however, when narcotics are used judiciously.

Any justification of the opposition to narcotics stems from experiences caused by their misuse rather than their widespread use. The routine use of narcotics without individualization obviously leads to difficulty, as will such use of any drug. Most difficulties have arisen when narcotics have been used in patients who should not have had them, when they have been used to excess to the point of inducing unconsciousness, or when they have been used and could have been omitted. Such misuse leads to the much complained of severe respiratory depression and hypotension. A common error is to administer the doses of narcotic ordinarily required for robust young patients to elderly patients. Elderly patients have less tolerance to central-nervous-system depressants than young or middle-aged persons. It is customary to reduce the dose of a narcotic to one-half, one-fourth, or even one-sixth of that required for middle-aged patients.

Most anesthetists obtain excellent sedation with use of a combination of morphine and scopolamine. Ten milligrams of morphine combined with 0.4 mg. of scopolamine administered subcutaneously one and one-half hours prior to anesthesia in an average adult produces tranquillity, an air of indifference, and amnesia without circulatory and respiratory depression. Consciousness is not lost, and the patient is able to converse, is aware of his environment, is relaxed, and is not anxious. The scopolamine enhances the cortical effects of morphine. As is the case with atropine, scopolamine appears to antagonize the depressant effect of morphine on the medullary centers.

The psychic sedation produced by the morphine-scopolamine mixture is superior to that of the morphine-atropine combination. Synthetic narcotics (methadone, alphaprodine [Nisentil], meperidine [Demerol]) are qualitatively similar to morphine but quantitatively different. They do not manifest the same intensity of sedative action and, therefore, do not relieve anxiety to the same degree as morphine. They may be used when morphine is not desired. Every experienced anesthetist knows that the morphine-scopolamine combination simplifies the technical management of inhalation anesthesia with nitrous oxide, cyclopropane, halothane (Fluothane), or ether.

Use of Ataraxics

Some anesthetists favor the combination of morphine and scopolamine fortified with an ataraxic, usually one of the phenothiazine type.[4] Phenothiazine derivatives produce an additive effect when combined with narcotics and hypnotics, so that the dose of the latter may be reduced and their side-actions minimized. However, phenothiazine derivatives introduce side-actions of their own which are more vexing and difficult to overcome than those of the narcotic. They produce varying degrees of ganglionic and sympatholytic blockade which result in a severe hypotensive state. Ambulatory psychiatric patients appear to tolerate continued therapeutic doses of phenothiazine derivatives without apparent serious consequences. However, when these patients are anesthetized or undergo operation, even under local anesthesia, hypotension of alarming proportions that is difficult to reverse may develop. Such hypotensive states have also occurred after the administration of single doses of a phenothiazine derivative for preoperative sedation.

Many anesthetists are reluctant to anesthetize any patient who has taken chlorpromazine or a phenothiazine derivative of similar potency within 48 hours of operation. Promethazine (Phenergan) is the mildest of this group and the one which manifests the least hypotensive effect. The drug was well established as an antihistaminic for some time before its tranquilizing effects were discovered. However, some anesthetists have reported the occurrence of mild hypotensive states during anesthesia when they have employed it preoperatively.[5] I have not encountered any such responses. Ataraxics of the propanediol (meprobamate), and diphenylmethane (hydroxyzine) type do not cause this hypotensive effect.

The efficacy of ataraxics used alone is not impressive. Promethazine used alone for sedation and amnesia is weak and ineffective. At times it tends to cause restlessness and mild excitement rather than tranquillity. It does, however, enhance the sedative action of narcotics, barbiturates, and other hypnotics and permits use of smaller doses of the latter. Perhaps in due time a suitable tranquilizer which will supplant the hypnotics and narcotics may be introduced. There is no such drug now.

Premedication in Children

Premedication for children poses problems because the response to premedicants is unpredictable and variable. A given regimen will produce a variety of responses in an apparently uniform group of subjects. In a certain percentage sedation will be adequate. In the others there will be either undersedation or oversedation. I and my associates[6] have used ataraxics, such as promethazine and hydroxyzine, with the narcotic hoping to eliminate this variability of response. These drugs do not, however, seem to accomplish this. Variability of response is as frequent with combinations of promethazine or hydroxyzine and a narcotic or a barbiturate and scopolamine as without the ataraxic. When equivalent doses are employed, as many patients appear undersedated or oversedated with the ataraxic combinations as without. The difficulty in premedication of children arises from inability to gauge individual doses.

Belladonna Alkaloids

Another aspect of premedication about which controversy occasionally arises is use of the belladonna alkaloids as antisecretory agents. Some practitioners oppose the preoperative use of these drugs because there are occasional side-actions. This objection is voiced most frequently by pediatricians who claim these drugs cause hyperthermia. Serious elevations in body temperature are uncommon. Flushing of the skin, particularly when atropine is used, occurs frequently in children. However, this is not associated with elevations in body temperature. The use of belladonna alkaloids is mandatory, particularly when inhalation anesthetics are used, to prevent secretion of mucus. Anoxia from respiratory obstruction is a more serious and far more frequent problem than hyperthermia.

From the time premedication was first suggested, atropine has been accepted as the conventional drug for this purpose. Other drugs are available which are superior, however. Atropine is a racemic mixture of tropine tropate. *Levo*-tropine tropate, also known as *levo*-hyoscyamine (Bellafoline) is the active physiological component of atropine. The *dextro* compound is physiologically inactive both as a vagolytic agent and as an antisialalogogue. When they are used in comparable doses, *levo*-hyoscyamine is almost twice as effective for suppressing the secretions as atropine.[7] Scopolamine (hyoscine) is equally as effective as *levo*-hyoscyamine for suppressing secretions. Its vagolytic action, however, is less than that of atropine and, therefore, it causes little or no changes in pulse rate. This is an advantage when acceleration in pulse rate must be avoided. In a group of volunteers, *levo*-hyoscyamine was found to cause an average increase in pulse rate of 25 per minute. Scopolamine caused none. Scopolamine enhances the tranquilizing and amnesic effect of a narcotic or hypnotic with which it is combined and at the same time produces the necessary drying effect. Also, it overcomes the tendency to nausea and emesis. Thus, scopolamine is a more desirable drug than atropine.

The synthetic anticholinergic drugs, such as oxyphenonium (Antrenyl), methantheline (Banthine), and methscopolamine bromide (Pamine), have little to offer over the belladonna alkaloids. They are less effective and desirable than scopolamine, atropine, or *levo*-hyoscyamine. Side-effects, such as extreme tachycardia and hyperthermia, have been reported when doses necessary to suppress secretions were used.[8] The synthetic anticholinergics have been promoted largely as spasmolytic drugs for gastrointestinal disorders because they appear to be devoid of antisecretory effects. Dryness of the mouth would be an undesirable side-action in a drug prescribed for this purpose. Thus, they are not intended for use in suppressing secretions. The majority of them appear to live up to the claim of their sponsors in this respect.

Vagal Blockade

The most frequent side-effect of anesthetics which requires the use of prophylactic agents with any degree of frequency is vagal excitation. This is most frequently observed during induction of anesthesia with halogenated hydrocarbons, such as chloroform, ethyl chloride, trichloroethylene, and halothane. Vagal effects of a less alarming degree occur with cyclopropane. Vagal excitation may occur reflexly from manual stimulation of thoracic and abdominal structures during operation. Atropine has been the conventional agent for suppressing such vagal activity. On a milligram-for-milligram basis, *levo*-hyoscyamine is more effective because it has a greater vagolytic action. Scopolamine is less effective than either atropine or *levo*-hyoscyamine as a vagolytic drug, particularly in regard to the cardiac portion of the vagus.

The recommendation that anticholinergic drugs be administered prior to thiopental anesthesia to obviate laryngeal spasm has been generally accepted. There is little scientific basis to support this practice. The vocal cords are composed of striated muscle and, therefore, are not affected by atropine and similar drugs which primarily block only postganglionic cholinergic fibers. Curare and allied muscle relaxants are more effective for overcoming laryngeal spasm. However, the belladonna alkaloids may be of benefit when thiobarbiturates such as thiopental and thiamylal (Surital) are used, because they inhibit bronchial activity. They may, thus, play a role in minimizing bronchial spasm, since bronchiolar activity is under parasympathetic control.

Potentiation of Anesthetics by Premedicants

Opinion is divided as to whether premedicants reduce the amount of the principal anesthetic needed for surgical anesthesia. Claude Bernard and Forné and others who pioneered premedication noted that induction of anesthesia was "smoother" when drugs were given preanesthetically and that less ether or chloroform was required to obtain surgical anesthesia. These clinical observations have been reiterated many times. Blood level studies appear to confuse the issue rather than clarify it, because the data of different investigators are not in agreement.[9] The electroencephalographic changes indicate that an additive effect occurs.[10] It has been well established from clinical experience that it is simpler to induce inhalation anesthesia with nitrous oxide and other agents in patients who have received premedication with morphine than in those who have had a hypnotic dose of a barbiturate or no premedication at all. Besides, concentrations of nitrous oxide necessary to maintain anesthesia are lower in patients who have had narcotics. The additive effect is more obvious when impotent anesthetics are used than when the more potent agents, such as ether or cyclopropane, are administered. Few will dispute the belief that the less potent anesthetic gases, such as nitrous oxide or ethylene, are more easily administered in combination with potent premedication agents.

Summary

Premedication should be considered part of the anesthetic. Psychic sedation, antisecretory activity, fortification of a primary anesthetic agent, and prophylaxis are the desired goals. In spite of a multitude of new drugs offered to anesthetists, the technique of premedication has changed little from that advocated by earliest workers. The narcotics in combination with belladonna alkaloids remain our most versatile, widely used, and reliable agents.

1532 Tulane Ave. (12).

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STUDY OF THE FREQUENCY AND DISTRIBUTION OF GLAUCOMA

Henry Packer, M.D., Alice R. Deutsch, M.D., Philip M. Lewis, M.D., Claude D. Oglesby, M.D.
and
Abraham C. Cheij, M.D., Memphis, Tenn.

Early recognition of impending or subclinical glaucoma offers hope of minimizing its role as a leading cause of blindness. In a glaucoma detection program, tonometer tests were applied to 13,155 persons who were undergoing examinations for complaints not immediately relating to the eyes. Glaucoma was found in 271 persons. The highest prevalence of glaucoma was in a hospital for the aged, where 36 cases (6.4%) of glaucoma were found among 562 inmates. Among 104 persons examined in an outpatient clinic and found to have glaucoma, 66 (64%) also had arteriosclerosis, and among 47 persons found to have glaucoma during examinations for employment health cards, 13 (28%) had arteriosclerosis. In general a high prevalence of arteriosclerosis, hypertension, arthritis, and syphilis was demonstrated among 151 persons found to have subclinical glaucoma. The inclusion of tonometry as part of the physical examination in patients over the age of 40 years or patients with chronic disease is recommended as a step toward the prevention of glaucoma.

Glaucoma is recognized as a disease for which no specific preventive measures are available, in view of its obscure etiology. The only hope of minimizing its role as a leading cause of blindness is through early diagnosis, preferably before the onset of overt symptoms. Fortunately the simple procedure of tonometry is available to screen out persons whose elevated intraocular tension makes them suspect of having this disease in the subclinical stage. This procedure is actually simpler than the screening tests in common use for the detection of such diseases as cancer, diabetes, or tuberculosis. A number of reports attest to the practicability and worthwhile results achieved when this test has been employed for mass screening of industrial and other population groups. However, in spite of the known serious consequences of neglected glaucoma and the frequent exhortation to physicians to include tonometry as a part of routine physical examinations, this procedure has not come into widespread use, either in the doctor's office or in public health case-finding programs.

Possibly more extensive practice of tonometry would occur if additional information were available regarding which segments of population are especially prone to have glaucoma, so that search for it could be carried out on a more selective basis. Attributes recognized as predisposing to this disease are inherited predisposition and age. Tonometry is generally recommended only for persons over 40 years of age, since glaucoma is uncommon in persons below this age. Other factors which might aid in more selective case finding for this disease need to be elucidated. Particularly is information needed regarding possible significant statistical association between glaucoma and other chronic diseases. That this occurs is frequently stated but poorly documented in the literature. Should such associations be established, either through retrospective or prospective studies, the practice of tonometry by physicians might be encouraged to a considerable degree by providing a more selective basis for such efforts than is the case at present.

This report presents information regarding the frequency and distribution of previously unrecognized glaucoma among various population groups obtained from a glaucoma detection program in which 13,155 persons were tested. The discovery rate varied considerably from group to group, and different attributes which appeared to influence this frequency will be discussed. Although some of this variation may be explained on the basis of chance,

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From the Division of Preventive Medicine and the Department of Ophthalmology, University of Tennessee College of Medicine.

the difference between some groups in the frequency of occurrence of glaucoma appears to be statistically significant, even though the reasons for this may not be entirely clear. These data are presented in the interest of promoting more selective case finding and more widespread practice of tonometry.

Groups Tested and Methods

A glaucoma detection program for the recognition of subclinical glaucoma was established in the outpatient department of the teaching hospital of the University of Tennessee College of Medicine in September, 1956. A glaucoma clinic had existed for many years prior to this in the outpatient department, but the advanced stage of the disease generally encountered in patients coming to this clinic led to the initiation of a detection program to promote earlier diagnosis and treatment. A preliminary report[1] of results achieved during the first eight months has already been made, and these data are not included in the present report, which is based on two subsequent years of testing.

During these two subsequent years, tonometer tests were routinely applied to persons over the age of 40 years in the following three categories: 1. Applicants for employment health cards. These were presumably well persons referred by employment agencies or employers. Negro women in domestic service constituted the largest proportion of this group. The Caucasian women were employed in food handling establishments mainly. Multiple screening procedures, including tests for uterine cancer, tuberculosis, diabetes, syphilis, and glaucoma, were performed in this group. 2. New admissions to various clinics of the outpatient department. These were persons with symptoms of illness coming to the clinic for diagnosis and treatment. Most of these persons were tested in the general medicine clinic or in medical specialty clinics while waiting to be examined. 3. Patients attending the ophthalmology clinic. Tonometry was routinely performed on such patients over 40 years of age. These patients were attending the ophthalmology clinic due to complaints relating to vision, and most of the glaucoma found in this group represents "clinical" glaucoma. This group is therefore indicated separately in the tables and not included in the total figures indicated for the detection program, whose purpose was to discover "subclinical" glaucoma.

Throughout the program, the testing of intraocular tension has been performed by a registered nurse who had received special training in the practice of tonometry by the staff of the ophthalmology clinic. She worked in proximity to the admitting office of the outpatient department and in various clinics of the division of medicine. Persons showing an intraocular tension of more than 25 mm. Hg with the Schiøtz tonometer were referred to the ophthalmology clinic for retesting and evaluation by the professional staff. Details of follow-up testing procedures have been described elsewhere.[1] Final evaluation of each suspect was carried out by an ophthalmologist who conducted a special evaluation clinic each week for the program. Hypersecretion and narrow angle mechanisms were studied by tonometry and gonioscopy in arriving at an evaluation.

Suspects were placed in the following categories on the basis of the criteria indicated. 1. Glaucoma. This was diagnosed on the basis of persistent abnormalities of intraocular tension, diurnal variations in intraocular tension, differences of 5 mm. Hg or more in intraocular tension between the two eyes, and positive water provocative or other provocative tests. 2. Borderline glaucoma. These patients showed two abnormalities, such as diurnal variations in intraocular tension beyond the normal range, slightly abnormal water provocative test results, or abnormally low tonographic C values (these are ratios describing the facility of outflow of the aqueous humor in four minutes). 3. Doubtful cases. Patients with one abnormal finding, such as slightly elevated intraocular tension, were asked to return for further observation.

TABLE 1.—*Frequency of Glaucoma in Various Groups*

	Persons Tested, No.	Persons with Glaucoma	
		No.	%
Employment health card applicants	2,516	45	1.8
Outpatient clinics	4,742	138	2.9
Shelby County Hospital	562	36	6.4
Nonhospital groups, total	5,335	52	1.0
Under 40 years	(1,027)	(2)	0.2
Over 40 years	(4,308)	(50)	1.2
Total	13,155	271	2.1
Ophthalmology clinic	902	62	6.9

During the first two years of the program testing was confined to the hospital groups mentioned above. Subsequently, tonometer testing was offered to employee groups in the community, such as school teachers, post office employees, department store employees, and employees in industrial plants. One reason for extending the testing program beyond the hospital group was that this group consisted mainly of Negroes, and information was also desired on Caucasians for comparison. Inmates of an institution for the aged (Shelby County Hospital) were also tested. In all, 13,155 persons were tested during the two years of the program, not including persons with eye complaints tested in the ophthalmology clinic. The same person tested hospital and nonhospital groups so that screening techniques for both might be considered uniform. Various ophthalmologists evaluated suspects in the nonhospital groups, who were referred to ophthalmologists of their choice whose diagnoses were accepted as final.

Analysis of Results

Table 1 presents data relating to the frequency of glaucoma in the various groups studied. Borderline cases of glaucoma are included, since experience has indicated that a positive diagnosis of glaucoma is ultimately made in most of these cases.

The highest prevalence of glaucoma (6.9%) was observed in persons attending the ophthalmology clinic. This is not surprising in view of the factor of selection operating in this group, namely, that these persons were already suffering from some visual disturbance which prompted them to seek medical attention. This represents the only group in which this factor played a role, and therefore this group is not included with the others in arriving at the total number tested in the detection program. The remaining groups were, to all intents and purposes, unaware of eye disease, and subclinical glaucoma was discovered in them as a direct result of the detection program. While the frequency of glaucoma was higher in the ophthalmology clinic group (6.9%) as compared to the outpatient clinic group (2.9%), the total number of new cases (138) of glaucoma found in the latter group was more than twice as high as in the former group (62). The employment health card applicant group also yielded many cases of glaucoma (45). These newly found cases in groups without visual complaints were obviously of earlier stages of the disease.

In the remaining groups the highest prevalence of glaucoma was observed in inmates of a county hospital for the aged. Thirty-six cases (6.4%) of glaucoma were found in 562 persons in this group. These cases were almost exclusively in persons over the age of 60 years and indicate the strong influence of age on the frequency of occurrence of glaucoma. This factor is also reflected in the smaller percentage (0.2%) of persons under 40 years of age in nonhospital groups found to have glaucoma as compared to persons over 40 years of age, who showed six times as much glaucoma (1.2%). Among the 5,335 persons in nonhospital groups tested, 1% were found to have glaucoma. This lower prevalence of glaucoma, compared to that observed in employment health card applicants coming to the hospital (1.8%), can be explained on the basis of other factors influencing prevalence. The frequency of glaucoma in the outpatient clinic group (2.9%) was significantly higher than that found in the health card applicant group (1.8%).

Table 2.–*Distribution of Glaucoma by Race, Sex, and Occupation in 11,566 Persons over 40 Years of Age*

	Caucasian						Negro					
	Male			Female			Male			Female		
		Glaucoma			Glaucoma			Glaucoma			Glaucoma	
Group	Tested, No.	No.	%	Tested, No.	No.	%	Tested, No.	No.	%	Tested, No.	No.	%
Employment health card applicants	153	0	0.0	515	7	1.4	316	6	1.9	1,532	32	2.1
Outpatient clinics	319	4	1.3	320	11	3.4	1,733	43	2.5	2,370	80	3.4
Teachers and department store employees	79	0	0.0	817	0	0.0	55	0	0.0	204	2	1.0
Other occupations	1,704	21	1.2	598	2	0.3	811	25	3.1	40	0	0.0
Total	2,255	25	1.1	2,250	20	0.9	2,915	74	2.5	4,146	114	2.7
Ophthalmology clinic	116	3	2.6	133	2	1.5	216	21	9.7	437	36	8.2

Table 2 shows the influence of race and sex and of a possible occupational factor on the frequency of subclinical glaucoma in persons over 40 years of age. These constitute the same groups as in table 1 except for the elimination of the nonhospital group under 40 years of age and the Shelby County Hospital group and the arbitrary separation of the nonhospital groups over 40 years of age into two categories. One category consists of 614 school teachers and 541 department store employees, whose work may be considered to entail considerable discriminatory use of the eyes with a minimum of physical activity. The other category consisted of persons employed in a lumber mill (284), a tire and rubber plant (890), shop workers in Army and Air Force depots (1,546), and mail carriers (433), whose work (in the case of males) entailed considerable manual labor with minimal eye strain. Some exposure to eye irritants was also observed in workers in the second category. It will be noted that most of the persons in this second category were Caucasian and Negro males. Also, the 598 Caucasian females included in this category were mainly office workers whose activities were more closely allied to those of the females in the first category than to those of the males in the second category. As in table 1, the data for the ophthalmology clinic group are listed separately and are not included in the totals for the detection program, for reasons already mentioned.

If the frequency of unrecognized glaucoma according to race and sex is examined for the total number of persons under consideration (11,566), a small difference is observed in incidence between Negro males (2.5%) and females (2.7%). The difference in the frequency of unrecognized glaucoma in Caucasian males (1.1%) and Caucasian females (0.9%) was not statistically significant. However, highly significant were differences observed between the frequency of unrecognized glaucoma in Negro males (2.5%) as compared to Caucasian males (1.1%) and Negro females (2.7%) as compared to Caucasian females (0.9%). While it is recognized that breakdown of the above groups by race and sex produces subgroups, some of which are so small that it is unjustifiable to draw broad conclusions from them with regard to distribution differences, certain of the latter are sufficiently consistent to warrant attention.

The higher prevalence of glaucoma in Negro than in Caucasian groups was particularly evident in the ophthalmology clinic group, where a fourfold to fivefold difference was noted for both sexes. For the other groups as a whole, the excess among Negroes was less marked but was more than twofold for males and more than threefold for females. The highest frequency of unrecognized glaucoma (3.4%) was observed in Caucasian females and Negro females in the outpatient clinic group. A somewhat lower percentage (3.1%) was observed in Negro males in the second category of the nonhospital group. Age adjusted rates are uniformly higher for Negroes of both sexes in all groups. These differences suggest that some fundamental factor is at work which either predisposes Negroes to glaucoma or operates to prevent its early recognition.

Surprisingly few cases (two) of unrecognized glaucoma were found in the first category of the nonhospital group which included school teachers and department store workers (1,155 persons). This finding may be partially explained by the high percentage (70%) of Caucasian females in this category. For the total groups, Caucasian females showed the lowest frequency of unrecognized glaucoma (0.9%). Only two previously unknown cases of glaucoma were uncovered by the examination of 1,415 Caucasian females in the two categories of the nonhospital group. These persons were school teachers, department store employees, and office workers in the industrial concerns mentioned previously. It is conceivable that the demands made on discriminatory vision by the occupation of these persons leads them to secure frequent examinations by ophthalmologists and therefore early recognition of glaucoma, thereby accounting for the small number of unsuspected cases found by routine testing. Information is not available regarding the number of persons already under treatment for glaucoma in these groups at the time they were tested, so this possibility cannot be verified.

The significantly higher frequency of glaucoma in the outpatient clinic group compared to the health card group led to inquiry regarding the frequency of other chronic diseases in these two groups. Table 3 indicates associated diseases found in 151 persons discovered to have glaucoma by our detection program. The clinic and hospital records of these persons were examined and the prevalence of the most commonly recorded diseases was determined. As would be expected, a higher prevalence of these diseases was noted in persons coming to the outpatient clinic for treatment than in those applying for employment health cards. Adjustment for age does not affect the magnitude of these differences.

The high incidence of diseases such as arteriosclerosis, hypertension, arthritis, and syphilis in our subclinical cases of glaucoma raises the possibility that common underlying mechanisms may play a role in pathogenesis. Duke-Elder's[2] concept of glaucoma as a "sick eye in a sick body" is brought to mind by these observations. Prospective studies are needed to document the frequency of glaucoma in its various stages in relation to chronic diseases of various types. Such information may help further to establish tonometry as an indispensable procedure in the physical examination of persons over 40 years of age coming to the physician's office.

Summary

The tonometer testing of 13,155 persons in hospital and nonhospital groups over a two-year period uncovered 271 persons with subclinical cases of glaucoma not under treatment. During the same period 62 persons who came to the ophthalmology clinic of the hospital with visual complaints were given a diagnosis of glaucoma.

The highest frequency of subclinical glaucoma was found in residents of a home for the aged (6.4%). The next highest frequency (3.4%) was found in Caucasian and Negro females visiting outpatient clinics. Negro males engaged in occupations involving considerable manual labor with minimal demands on discriminatory vision ranked next (3.1%).

The lowest frequency of subclinical glaucoma was observed in Caucasian females engaged in occupations requiring discriminatory visual activity.

For the total groups tested subclinical glaucoma was found over twice as frequently in Negro males as in Caucasian males and three times as frequently in Negro females as in Caucasian females. This excess frequency in Negroes was even more marked with reference to clinical glaucoma diagnosed in persons visiting the ophthalmology clinic.

TABLE 3.—*Associated Disease in 151 Persons with Glaucoma Discovered by Detection Program*

	Outpatient Clinics (104 Persons)		Employment Health Cards (47 Persons)	
Disease	No.	%	No.	%
Arteriosclerosis ...	66	63.5	13	27.7
Hypertension	52	49.0	10	21.3
Arthritis	28	26.9	8	17.0
Syphilis	20	19.2	7	14.9

A high prevalence of arteriosclerosis, hypertension, arthritis, and syphilis was observed among 151 persons with subclinical glaucoma found by the detection program.

The above observations point the way to more selective case finding procedures where resources are limited and suggest that tonometry should be made an indispensable procedure in the examination of persons over 40 years of age in general and in persons with chronic illness in particular.

62 S. Dunlap St. (3) (Dr. Packer).

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CLINICAL NOTES

CONGENITAL PULMONARY CYSTIC LYMPHANGIECTASIS

Jordon Frank, M.D.
and
Philip G. Piper, M.D., Madison, Wis.

It is generally held that congenital cystic disease of the lung is of bronchial origin. However, since Virchow[1] first described a similar lesion, thought to be of lymphatic origin, 21 such cases have been reported in the world literature. We wish to add two additional cases, one of which presents an unusual association of lymphatic cystic dilatation in other body organs.

As is often the case with new lesions, there are divergent points of view as to their etiology and the terminology to be applied to them. Laurence[2] described congenital cystic disease of the lung as congenital pulmonary cystic lymphangiectasis, Giammalvo,[3] as congenital lymphangiomatosis of the lung, and Maidman and Barnett,[4] as congenital dilatation of pulmonary lymphatics.

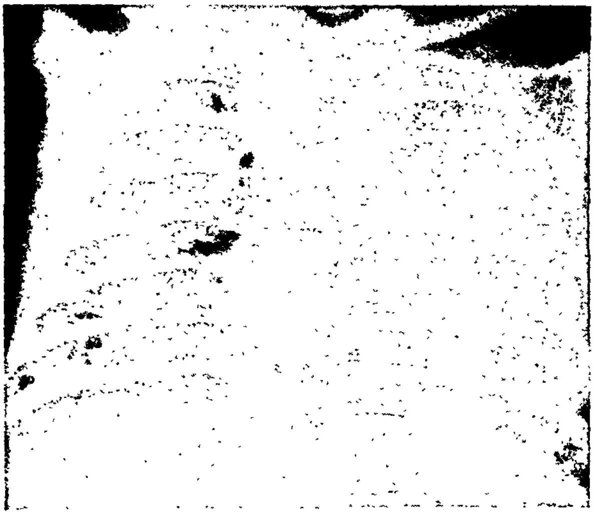

Fig. 1 (case 1).—Chest roentgenogram showing bilateral multiple scattered densities representing cystic spaces found at autopsy.

It is apparent from a review of all cases that this entity, no matter by which name it is called, must be included with other disease processes responsible for neonatal cyanosis and, unfortunately, can be positively identified only by means of autopsy.

Report of Cases

Case 1.—A 23-year-old primigravida, whose prenatal course was uneventful, gave birth to a full-term baby girl which was delivered by low forceps, without complications. The baby cried well and looked healthy at first, but 10 minutes later became limp and cyanotic, with sluggish, grunting respirations. It was treated with caffeine and sodium benzoate and placed in an infant incubator (Isolette) with oxygen. An x-ray of the chest was taken and revealed bilateral multiple scattered densities (fig. 1). The child did not respond to the above therapy and died approximately two hours after birth.

An autopsy was performed one hour after death. The body was that of a well-developed, mature female newborn infant weighing 3,240 Gm. (7 lb. 2 oz.), with a crown-to-heel measurement of 54 cm. (1 ft. 9.2 in.). No external anomalies were present. The pleural cavities were free from fluid, and there was approximately 3 cc. of a clear, straw-colored fluid present within the pericardial cavity. The left lung weighed 22 Gm. and the right lung, 26 Gm. All lobes contained subpleural cystic areas, the largest of which measured 6 mm. in diameter. The lung parenchyma was soft and pink, with markedly decreased crepitation and diffuse pinpoint cystic spaces. A moderate amount of serous fluid could be expressed from the lung parenchyma. Not only the pulmonary vasculature, hilum, and tracheobronchial tree but also the remaining organs were unremarkable on gross examination.

Microscopic examination of the lungs revealed the presence, in all lobes, of multiple cystic spaces and dilated channels, lined by flattened cells that appeared to be endothelial in type and supported by variable amounts of fibrous connective tissue. These cystic spaces and dilated channels were in close approximation to the pulmonary vasculature (fig. 2) and occurred predominantly in three areas: subpleurally, between the connective tissue septa of the lung, and peribronchially. There was no evidence, in multiple sections, of any connection with either arteries or veins. For the most part these dilated channels and cystic spaces were empty, except for an occasional erythrocyte and leukocyte. The pulmonary vasculature and bronchi were unremarkable, and the lung parenchymal tissue was diffusely atelectatic, with the exception

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Chief of Pathology and Director of Laboratories, Madison General Hospital, and Assistant Clinical Professor of Pathology, University of Wisconsin School of Medicine (Dr. Piper); Resident, Department of Pathology, Madison General Hospital (Dr. Frank).

of a few dilated respiratory bronchioles and alveolar ducts. There was a minimal to moderate degree of vascular congestion, as well as an occasional area of perivascular hemorrhage. The remaining organs were unremarkable, except for vascular dilatation and congestion.

Case 2.—A full-term, hydropic male stillborn infant was delivered, by low forceps, from a 23-year-old primigravida whose prenatal course had been uneventful. An autopsy, performed three hours after the stillbirth, showed the body to be that of a well-developed, mature, hydropic baby weighing 4,820 Gm. (10 lb. 10 oz.), with a crown-to-heel measurement of 53 cm. (1 ft. 8.9 in.). There was marked, generalized edema, with a large protuberant abdomen. While there was no evidence of trauma or of external anomalies, there was approximately 150 cc. of a clear, yellow fluid within each of the pleural cavities as well as 5 cc. of a similar fluid within the pericardial cavity. The left lung weighed 12 Gm. and the right lung, 14 Gm. Bilateral atelectasis was present, and the lungs were soft, pink, and noncrepitant. Laryngeal edema was marked; however, the tracheobronchial tree was patent throughout. The pulmonary vasculature and hilum were grossly unremarkable, as was the heart, and no cardiovascular anomalies were present. The diaphragm was flattened and located at the seventh intercostal space bilaterally. There was marked edematous thickening of the anterior abdominal wall. The abdominal cavity contained 300 cc. of a clear, yellow fluid, and the viscera were in their usual positions in situ and grossly unremarkable. There was also marked edematous thickening of the soft tissue of the scalp, with small scattered focal areas of hemorrhage over the parietal and occipital regions bilaterally. There were no fractures of either the calvarium or the base of the skull. The brain showed no evidence of trauma, contusion, or laceration, but there was marked cerebral edema and moderate congestion.

Microscopic examination of the lungs revealed the presence, bilaterally, of multiple cystic spaces and dilated channels lined by flattening endothelial-type cells, supported by varying amounts of fibrous connective tissue. Except for the size of these cystic spaces, the histological picture here was similar in all respects to that described in the first case, with the additional evidence of developmental retardation of the lung parenchymal tissue (fig. 3). The heart, pancreas, kidneys, and mesenteric tissue contained cystically dilated, endothelial-lined channels within the interstitial tissue of these organs, similar in appearance to the cysts and dilated channels present in the lungs (fig. 4). A section of the anterior abdominal wall revealed a marked diffuse edema of the soft tissues; however, no dilated channels were present. The remaining organs showed moderate vascular congestion. The etiology of the hydropic condition of this baby was undetermined; serologic and microscopic examinations showed no evidence of Rh incompatibility.

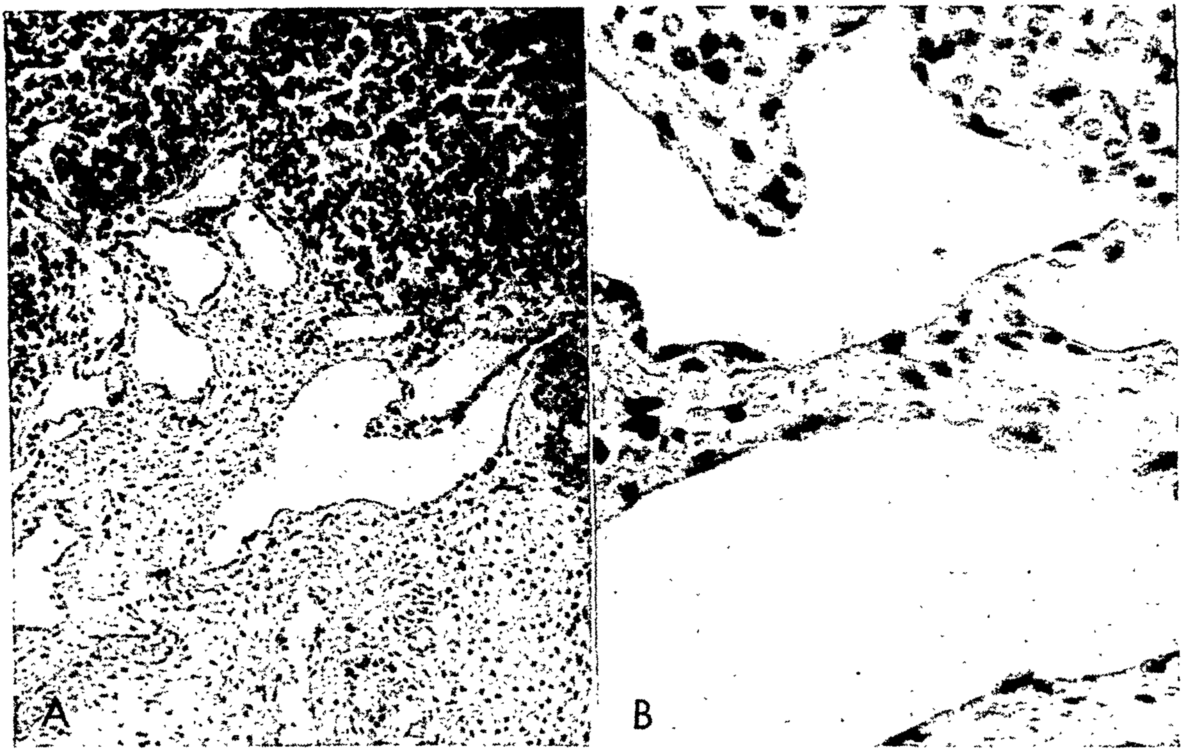

Fig. 2 (case 1).—*A*, microscopic section of lung showing cystic dilatation of lymphatics in peribronchial septum (× 75). *B*, microscopic section of lung showing endothelial lining of cystic spaces (× 825).

Comment

In both of these cases the pulmonary cysts occurred in positions where the lymphatics are located and, in many instances, connected with what appear to be dilated lymphatic channels. In none of the sections could these cysts and dilated channels be found connecting with either the vasculature or the bronchi. In addition, the composition of the cysts and channel walls resembles the walls of lymphatics.

According to the literature,[5] *this condition has* been described only in fetuses and newborn infants and is most likely congenital in origin. It is felt that this represents a primary disorder of development, as opposed to a secondary lymphangiectasis due to obstruction, since no obstructive lesion has been demonstrated in any of the previously reported cases, nor in our two cases. Published reports [6] of lymphangiectasis associated with obstructive lesions describe the lymphatic vessel walls as containing a large amount of muscle fiber and connective tissue proliferation associated with chronic inflammatory cell infiltration. Similar findings are present in filarial elephantiasis. However, in cases of congenital pulmonary lymphangiectasis, none of these changes is noted.

In over one-half of the autopsies performed in cases of congenital pulmonary lymphangiectasis, other major congenital malformations do occur.[2] A review of the embryology of the lung leads us to the supposition that this entity is one of maldevelopment. In about the ninth week of fetal development lymphatics grow into the lung bud and then rapidly expand. The exact mode of development of the lymphatic system is undecided.[7] Huntington and McClure [8] favor the origin of the lymphatic system from a progressive fusion of isolated mesenchymal spaces, while Sabin [9] favors the origin of lymphatic endothelium from proliferation of preexisting endothelium. During the 12-to-16-week stage, the lymphatic system in the lungs is well developed and divides the pulmonary parenchymal tissue into fairly distinct lobules.[10] From the 18th to the 20th weeks the connective tissue diminishes in amount, and the lymphatics become narrower, resulting in decreased prominence of the lobulations of the lung. Laurence [2] states that congenital pulmonary lymphangiectasis represents a continued growth of the lung, with the tissue elements maintaining their 12-to-16-week proportions, and thus possibly accounting for the normal development of the lung parenchyma. Giammalvo,[3] however, accepting the premise that the lymphatic system originates from isolated mesenchymal clefts, feels that the cystic dilatation of the lymphatics results from the failure of or delay in linkage of isolated lymphatic spaces. Laurence,[2] however, infers that if this were the explanation, then cysts would be more likely confined to the peripheral portions of the lungs, where fusion occurs last. Since the distribution of this entity is diffuse, and since in Laurence's study of serial sectioning and reconstruction these cysts are shown to form a network of intercommunicating channels, he thus postulates his theory of developmental arrest at the 12-to-16-week stage.

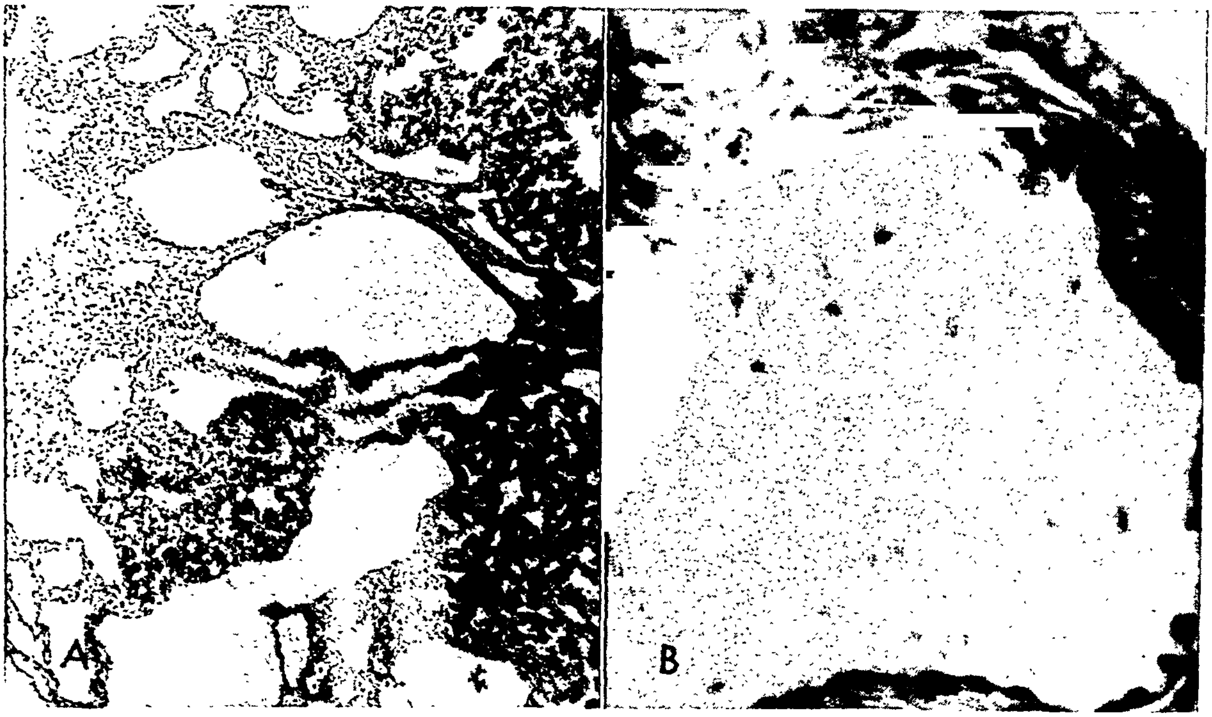

Fig. 3 (case 2).—*A,* microscopic section of lung showing multiple cystic spaces within pulmonary septa (× 75). *B,* microscopic section of cystic spaces in lungs showing lining endothelium (× 825).

According to Laurence,[2] congenital pulmonary lymphangiectasis should be differentiated from cases in which pulmonary lymphatic cysts are part of a generalized lymphatic disorder throughout the body. McKendry and associates,[11] in their discussion of a generalized lymphatic disorder, include idiopathic chylous ascites, chylothorax, or lymphedema as one of the manifestations. These have occurred in older infants ranging from 5 weeks to 5 months of age. Since none of these conditions was present in our second case, we feel that congenital cystic lymphangiectasis, which in all previous reports had been confined to the lungs, can occur as a generalized disorder. The histological

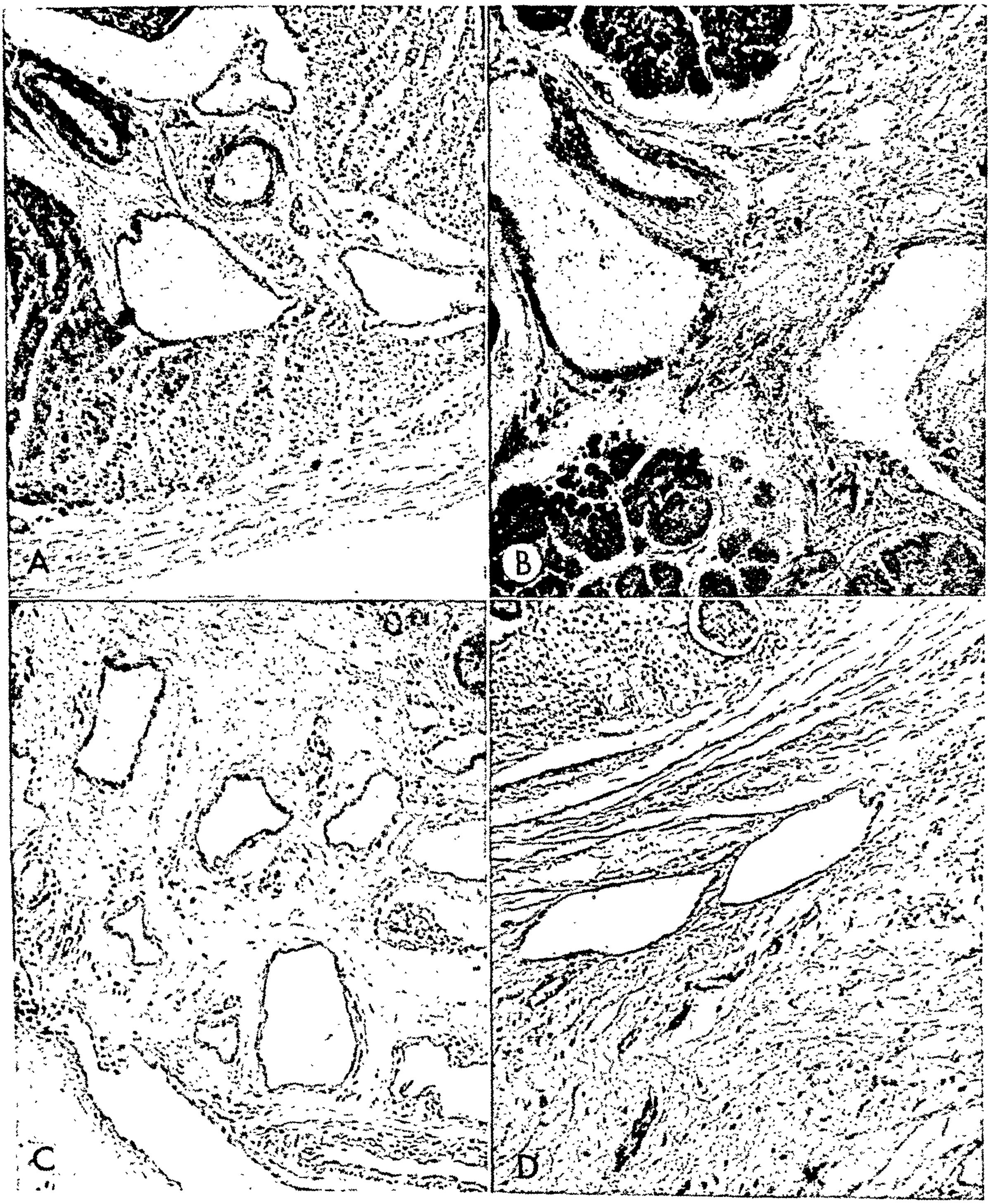

Fig. 4 (case 2).—*A*, microscopic section of heart showing cystic spaces in interstitial connective tissue of myocardium (× 75). *B*, microscopic section of pancreas showing cystic lymphatics in interstitium. C, microscopic section of mesentery showing dilated lymphatics. *D*, microscopic section of kidney showing cystic lymphatics in peripelvic connective tissue (× 75).

appearance of the cystically dilated lymphatics in the other organs is similar in all respects to that present in the lungs.

It is interesting to speculate on the increased incidence of this lesion since 1955. Could it be due to more accurate recognition, a higher rate of autopsies performed on neonatal and stillborn infants, or to an actual rise in some causative agent or agents—toxic, bacterial, or viral—in the mother?

Summary

As revealed by autopsy and histological resemblances, congenital pulmonary lymphangiectasis can be associated with lymphangiectasis in other organs. Our assumptions concerning the possible pathogenesis concur with Laurence's concept that this entity represents a primary developmental malformation of the lymphatic system, resulting in irregular cystic dilatation of the lymphatic vessels.

Although it occurs predominantly within the lungs, it can be part of a generalized primary disorder. As such it is distinct from the secondary type of lymphangiectasis associated with obstructive lesions, as well as from the generalized lymphatic disorders occurring in older infants.

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We are indebted to Miss Merian Smith for the technical assistance provided.

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SPONTANEOUS DISAPPEARANCE OF GALLSTONES

Joseph F. Linsman, M.D.
and
Eliot Corday, M.D., Beverly Hills, Calif.

The following case report presents a unique instance in which sizable multiple gallstones disappeared during a four-year interval without any history of biliary colic, jaundice, or other episode that would suggest the formation of a fistula between the gallbladder and some other part of the intestinal tract.

Report of a Case

The patient was a 65-year-old man, who in 1953 had complained of pain in the left side of the chest on slight exertion, with radiation down the left arm. Because of this precordial distress he was unable to perform his routine duties. On three occasions in 1953 and 1954 the patient had to be hospitalized for paroxysms of rapid auricular tachycardia or fibrillation. At the time of the paroxysms he experienced severe precordial distress and his blood pressure dropped to hypotensive levels. On each occasion the paroxysms of tachycardia were converted within a few hours to regular rhythm by the administration of lanatoside C (Cedilanid) intravenously.

In July, 1954, the patient's radioactive iodine (I^{131}) uptake was 39.4%; blood iodine level, 5.4 mcg.%; blood cholesterol level, 204 mg.%; hemoglobin concentration, 16 Gm.%; white blood cell count, 5,400 per cubic millimeter; urinalysis, normal; sedimentation rate, 6 mm. per hour; and uric acid level, 4.2 mg.%.

The electrocardiogram was within normal limits; however, during the paroxysms of tachycardia, the patient developed S-T segment depression and T-wave changes. He appeared euthyroid. On Oct. 12, 1954, cholecystography revealed a normal concentration of the opaque medium (iopanoic acid, 3 Gm.), and within the gallbladder there were 10 rounded negative shadows, measuring 7 to 9 mm. in diameter, with an appearance characteristic of gallstones. With the patient in the upright position

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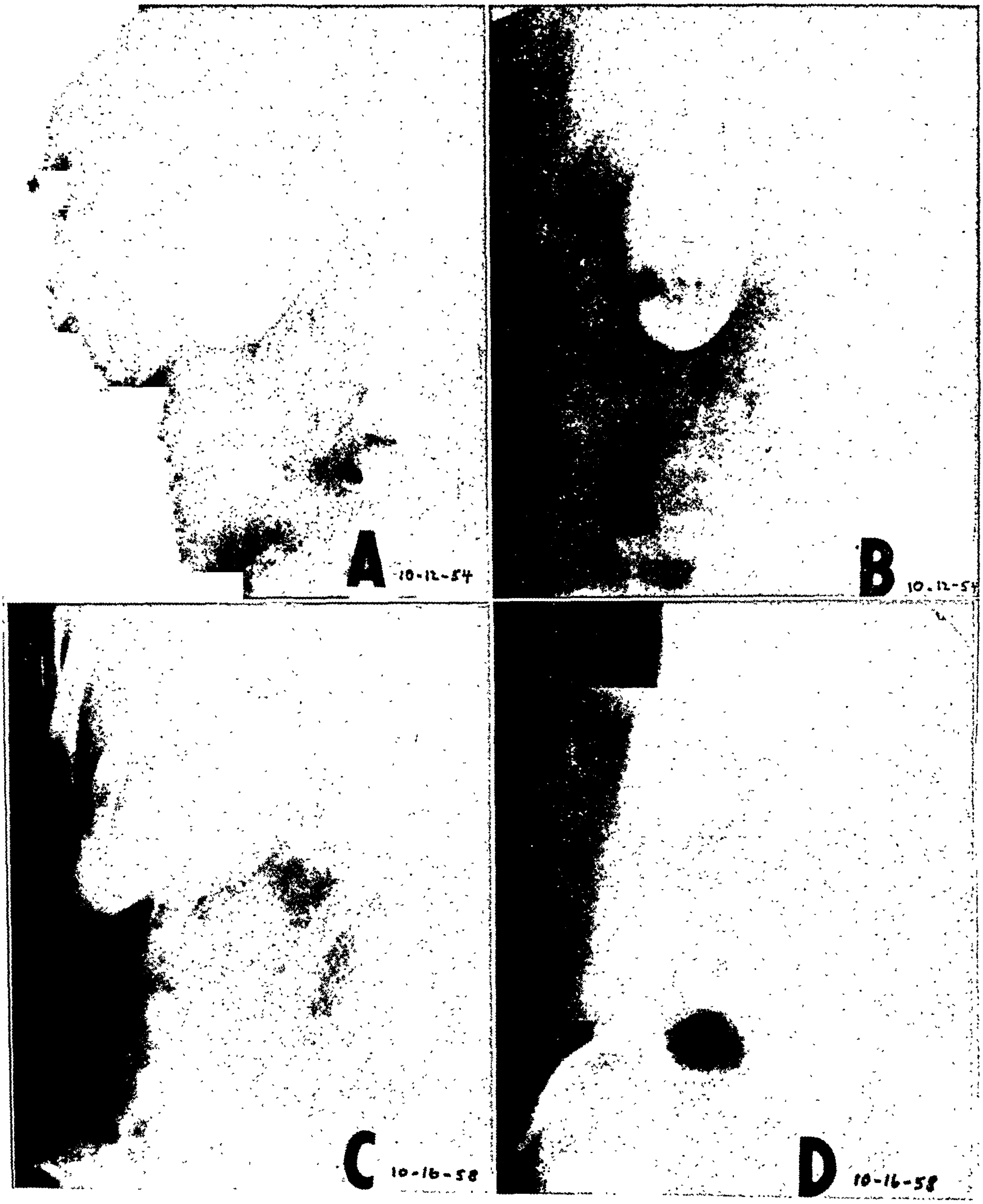
Associate Clinical Professor of Radiology, College of Medical Evangelists (Dr. Linsman), and Assistant Clinical Professor of Medicine, University of California (Dr. Corday), Los Angeles.

these appeared to be in layers. This study also revealed an enlarged right kidney shadow (see figure, *A* and *B*).

Radioactive iodine was administered, because the episodes of tachycardia or fibrillation, which were not responding to antiarrhythmic agents, were becoming more frequent and because the angina of effort was more disturbing. The patient was given 12 mc. of radioactive iodine in divided doses. His angina of effort gradually disappeared over a three-month period, and he was able to resume his routine duties as a vascular surgeon. His blood choles-



A, cholecystogram made Oct. 12, 1954, with patient in recumbent position, showing 10 radiolucent gallstones; *B*, cholecystogram made same day with patient in upright position. Note layered appearance of gallstones. *C*, normal cholecystogram made Oct. 16, 1958, with patient in recumbent position; *D*, cholecystogram made same day with patient in upright position. Note absence of gallstones. Studies made both dates show same enlarged right kidney, so possibility of patient mix-up was excluded.

terol level rose to 240 mg.%. The patient did not experience any recurrence of the tachycardia after that time.

In November, 1955, the patient again started to experience angina of effort. His radioactive iodine uptake at this time was 27.8%. An additional 18 mc. of I^{131} was administered in three divided doses. The patient has not experienced any angina since January, 1956. In October, 1958, the protein-bound iodine level was 1.8 mcg.% and the blood cholesterol level 210 mg.%. The electrocardiogram did not reveal any significant change. During a routine physical examination the enlarged right kidney was palpable. Intravenous urography demonstrated large cysts of both the upper and lower poles of the right kidney. Cholecystography on Oct. 16, 1958, revealed no evidence of the previously visualized nonopaque gallstones. The gallbladder appeared entirely normal, in roentgenographic studies made with the patient in the recumbent and upright positions (see figure, *C* and *D*).

A comparison of the gallbladder studies of Oct. 12, 1954, with those of Oct. 16, 1958, revealed the right kidney enlargement to be present in both examinations, thereby excluding the possibility that a patient mix-up might account for the absence of calculi in the later study.

Comment

Spontaneous cures of radiographically demonstrated gallstones have been reported. One of these reports[1] deals with a 23-year-old woman who had attacks of biliary colic during pregnancy. Two weeks after delivery a cholecystogram revealed numerous, clearly delineated radiolucent calculi which measured 2 to 3 mm. in size. No further colic occurred thereafter. However, at laparotomy seven weeks later, the gallbladder and the bile ducts contained no calculi.

Another instance was reported by Kommerell and Wolpers.[2] Their patient showed unequivocal radiolucent gallstones of various sizes. Of the stones 21 were small, measuring up to 5 or 6 mm. in diameter, and 3 were larger, measuring up to about 10 mm. in diameter. Roentgenologic studies were repeated at almost yearly intervals, and these revealed that the stones became gradually smaller but no fewer, and, after six years, no stones could be demonstrated by cholecystography. This patient had no biliary colic during the six-year interval.

Ortmayer and Austin[3] reported on three patients in whom gallstones were recovered from the feces, but all of their patients had typical attacks of biliary colic associated with jaundice. Moreau and Moreau[4] reported a case in which calcified gallstones were demonstrated radiographically. Later studies showed their complete disappearance from the gallbladder after an 11-year interval. Some of these stones were shown on their roentgenographic studies to be passing through the common duct. Eventually the cholecystogram was normal. Their patient had frequent attacks of colic and jaundice.

Our case clearly demonstrated that gallstones of the radiolucent variety can disappear spontaneously. It seems unlikely that they did so by migration, without either colic or jaundice. Furthermore, since the patient was a physician, any episode which would have given rise to fistula formation between the gallbladder and the intestinal tract would have been noted by him or his medical attendants.

Since one of the causes of nonopaque gallstones is related to disordered cholesterol metabolism,[5] one conjectures whether further alteration of the cholesterol metabolism in our patient may have had something to do with the disappearance of his gallstones. The administration of radioactive iodine to this patient for his coronary artery disease was quite effective, and he became hypothyroid and required administration of thyroid. There may have been mobilization of the patient's cholesterol stores during the induction of the hypothyroid state.

The gallstones in this patient measured from 7 to 9 mm. in diameter. Although it is known that calculi of this size may pass the relaxed sphincter of Oddi,[6] it is most unlikely that 10 such stones could have passed without the presence of biliary colic. Miller's[1] patient, who showed no stones at laparotomy after unequivocal demonstration of their presence seven weeks before surgery, had no biliary colic during this seven-week interval. However, the stones in that case measured at most from 2 to 3 mm. in diameter. Hypothyroid persons are alleged to have a higher than average pain threshold, but our patient gave no evidence that his pain threshold was sufficiently increased to permit biliary colic to go relatively unnoticed.

Summary

In an unusual case of biliary calculi there was disappearance of 10 sizable gallstones from the patient's gallbladder, without colic, jaundice, or other abdominal crisis.

436 N. Roxbury Dr. (Dr. Linsman).

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ANAPHYLACTOID REACTION TO VANCOMYCIN

Herbert J. Rothenberg, M.D., Denver

Vancomycin (Vancocin) hydrochloride is a potent antibiotic which is bactericidal for many strains of micrococci. As experience with the use of this drug has been obtained a variety of untoward effects have been observed. Notable among these have been febrile reactions and occasional hypotensive episodes. Eosinophilia, dermatitis, deafness, pruritus, and phlebitis from the infusion also have been reported. Occasionally chills followed infusion of the early batches, but this reaction no longer commonly occurs.[1] The following case illustrates a type of reaction which has hitherto been unreported but of which the clinician should certainly be aware.

Report of a Case

The patient was a 17-year-old girl known to have rheumatic heart disease. This disease had been inactive since the patient was 10 years of age and mitral insufficiency was clinically her only valvular lesion. For the past two years she had taken penicillin G orally, 250,000 units twice a day, as prophylaxis against streptococcic infections. She was a high school student who worked part-time in a hospital carrying food trays to patients. About two weeks prior to admission she scratched a "pimple" on her back, which then ceased to bother her. Two days prior to admission she suddenly developed weakness, nausea, generalized aching, shaking chills, headaches, and temperature of 39.5 C (103.1 F). These symptoms continued and she was admitted to the hospital on the third day of her illness with localized muscle tenderness in her right thigh, left buttock, and right shoulder and a 5-ml. erythematous tender indurated nonsuppurative lesion on her right thigh. She had one petechial lesion on her left palpebral conjunctiva, one on her soft palate, and a few scattered petechiae on her hands and around her ankles and shins. Her spleen was tender but difficult to palpate because of the guarding of her abdomen. She had a heart murmur that indicated mitral insufficiency which was unchanged from that previously described. The white blood cell count was 6,550 per cubic millimeter, with 83% polymorphonuclear neutrophils, 2% stab forms, and 15% lymphocytes. The urine was normal. History was pertinent only in a history of a skin rash necessitating the discontinuation of a sulfonamide preparation which had been used in prophylactic therapy four years before. There was no other drug or other type of allergy known and no personal or family history of asthma.

The condition of this patient was extremely toxic on admission and became more so with temperature spiking up to 40.7 C (105.3 F). A presumptive diagnosis of acute bacterial endocarditis was made and six blood cultures were drawn in the first 12 hours after admission. The severe nature of the illness seemed to make early antibacterial therapy mandatory and it was believed that it was not justified to await the outcome of the blood cultures. Two assumptions were made as to the nature of the offending organism, both of which subsequently proved to be correct: first, in view of the explosive nature of onset of this illness, that it was likely to be due to a staphylococcus; second, due to her chronic ingestion of small doses of penicillin and her daily contact with hospital patients discharging a variety of organisms, that the organism, whatever it was, was most likely resistant to penicillin. The blood cultures all eventually grew staphylococcus (Micrococcus) pyogenes var. aureus. Vancomycin was selected as a potent bactericidal agent useful against the anticipated type of organism.

After having received no therapy except aspirin, she was given an intravenous infusion containing 1 Gm. of vancomycin in 250 cc. of 5% dextrose in water in a total time of 25 minutes. She tolerated the infusion well and the needle was withdrawn. About 10 minutes after the infusion was concluded she suddenly developed chest pain, dyspnea, generalized pruritus, urticaria on her arms, back, and chest, and swelling of her face, lips, and eyelids. She was noted to be cyanotic, with cold extremities and a "barely palpable" radial pulse. Auscultation of the chest was not performed and blood pressure was not obtained. She was immediately given 0.2 cc. of aqueous epinephrine 1:1,000 intravenously and 0.3 cc. of the same medicament subcutaneously and oxygen was administered by mask. Examination 15 minutes later revealed her to be symptom-free except for sinus tachycardia (pulse rate of 120 beats per minute) and palpitation. A slight high-pitched expiratory wheeze was audible throughout her chest. She was given diphenhydramine (Benadryl) hydrochloride orally and suffered no further ill-effects. Therapy was then changed and she received no further vancomycin.

Comment

It is clear that the reaction described was the result of the administration of vancomycin. It is of interest for two reasons: First, this was an anaphylactoid reaction which occurred after the first dose

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From the Department of Medicine, General Rose Memorial Hospital and the University of Colorado Medical Center.

of the offending drug. Second, it is the first reaction of this type to be reported for this particular drug. The patient involved was a girl whose only known allergic history was sensitivity to a sulfonamide. Subsequently she developed an allergic reaction to novobiocin. The reaction experienced with vancomycin was one of major severity and was potentially fatal. The actual incidence of this type of reaction cannot be estimated at the present time, since experience with this drug has been limited. This should not prevent the use of vancomycin when the indications are clear. The fact that this reaction can occur should underscore the principle that potent drugs must be used with discretion and only with proper indication.

West Sixth and Cherokee streets (4).

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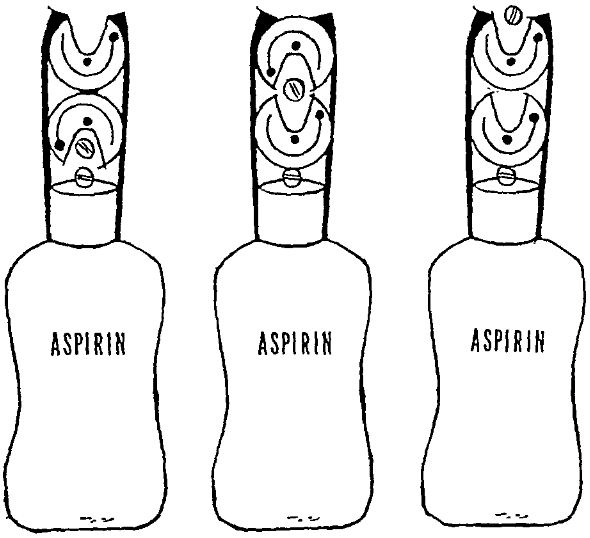
SAFETY ATTACHMENT FOR ASPIRIN BOTTLES

Robert Cohen, M.D., Bakersfield, Calif.

About two years ago a symposium on children's poisons was held at the Los Angeles Children's Hospital. The moderator, Dr. A. Parmelee Sr., allowed me to exhibit various devices for attachment to aspirin bottles as aids in the prevention of aspirin poisoning.



Safety attachment for aspirin bottles, showing rotation of wheels.

I stated that for economic reasons the manufacturers will not change the design of the bottles, but they are willing to consider safety attachments to the necks of the bottles. There are some ingenious devices on the market today, but all involve the cap's coming off every time an aspirin is used, which has one big drawback; that is, failure of the parents to replace the cap. The device herein introduced takes that into consideration, as well as the short attention span of a child. Also, puzzles and combinations are confusing and out of most children's mental grasp.

The device (see figure) has two adjacent plastic wheels, each wheel with a hollow U of a size sufficient to hold a standard aspirin cut into it, mounted on a firm plastic case. One plastic side has a circular groove over each wheel to guide the inserted pin, with a round knob attached in order to rotate the wheels. After the aspirin bottle is filled this plastic device is sealed to the neck with the standard collodion sealing material found on many bottles today.

In order to operate this safety attachment the wheel nearest the mouth of the bottle is rotated so that its U will be facing the mouth of the bottle. When the bottle is turned upside down it receives the aspirin tablet. Then this wheel, farther from the neck, is rotated so that its U faces the inside. The first wheel is rotated 180 degrees, the bottle is again inverted, and the aspirin tablet drops into the second wheel's U, which is again rotated 180 degrees and expels the aspirin tablet.

A child will turn the bottle upside down and will turn the small knobs but will seldom be clever enough to understand the combinations which release the aspirin tablets. This attachment should lower the incidence of aspirin poisoning.

2415 Niles St.

COUNCIL ON FOODS AND NUTRITION

The Council has authorized publication of the following report.

PHILIP L. WHITE, SC.D., *Secretary.*

DETERIORATION OF VITAMIN D WHEN MIXED WITH CALCIUM SALTS

Elmer M. Nelson,† Ph.D., Washington, D. C.

It has been known for fully 25 years that vitamin D is not stable when mixed with a preparation containing 25% or more of minerals. In 1932, the observation was made that, when mixed with limestone, cod liver oil did not retain its vitamin D.[1] Cod liver oil was added to ground limestone and the mixture stored in glass jars in the laboratory. When examined two weeks later, the mixture was devoid of the vitamin. With further investigation, researchers found that cod liver oil lost vitamin D rapidly when added to a salt mixture containing all of the mineral elements necessary for growth of the rat. However, the loss was just as rapid when the oil was mixed with a preparation of silica of the same degree of fineness. Loss of vitamin D at temperatures ranging from 85 to 100 F was more rapid than at room temperature, and less rapid in mixtures kept under refrigeration. Since no catalytic effect of the minerals could be demonstrated, it was concluded that the loss was due primarily to the greater surface area and a resulting increased exposure to air.

Since that time, we have examined a large number of vitamin D preparations on the market containing various calcium salts. In a sample of 50 preparations we assayed, 4 were devoid of vitamin D entirely, 5 had an excess of vitamin D of 100% or more, 20 contained a substantially greater excess of vitamin D than did the nonmineral vitamin D products, and the remainder were of satisfactory composition at the time of examination. Both vitamin D_2 and vitamin D_3 have been found, frequently in combination with di-calcium phosphate, but a variety of other salts and salt mixtures have been used. Products of this type generally are offered for use during pregnancy and are prescribed to a considerable extent by dentists.

The annual report of the Federal Security Agency for 1948 carried this statement: "Vitamin D is generally regarded as stable, but it deteriorates rapidly in the presence of minerals. This fact was first observed many years ago in mineral feeds, and feed manufacturers are now generally aware of the difficulty. Some pharmaceutical manufacturers continue to incorporate the calcium phosphate and other minerals in vitamin D tablets. Almost invariably these products are found low in vitamin D within a month or two of the time of manufacture."

Since that report was published, there have been some important developments, but at the present time the situation is far from satisfactory. Some manufacturers have tried to compensate for this deterioration by adding vitamin D in excess of the amount declared, but this is not a practical method of providing a satisfactory product due to the uncertain rate of loss. About two years ago, different forms of the so-called stabilized vitamin D came into use. The vitamin D in powdered form is coated in such a way that it is protected from air, even when used in a powdered mineral preparation. We do not know how well these coated preparations withstand the pill-making process in which the walls of the coated particles conceivably may be ruptured.

Pharmaceutical manufacturers usually have been prompt in discontinuing distribution of unsatisfactory preparations, but some have been reluctant to do so. With a chemical method for detection of vitamin D now available,[2] there should be no reason for continued distribution of unstable products of this type.

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From the Division of Nutrition, Food and Drug Administration, Department of Health, Education, and Welfare.

†Dr. Nelson died Dec. 24, 1958.

FELLOWSHIPS FOR RESEARCH IN CLINICAL NUTRITION

The Council has authorized publication of the following announcement. These fellowships are sponsored by the Nutrition Foundation, Inc., in cooperation with the Council. In 1960, 10 fellowships will be given in honor of Dr. Carl V. Moore, recipient of the 1959 Joseph Goldberger award in clinical nutrition.

PHILIP L. WHITE, SC.D., *Secretary.*

PURPOSE.—To stimulate staff members and students of schools of medicine to take a more active interest in the science of nutrition.

AMOUNT.—$200 per month for three months.

CONDITIONS.—1. Grant shall be made to a medical student on recommendation of a senior investigator. 2. Recipient will be selected by the Council. 3. Grant shall be used solely for remuneration of selected medical student. 4. Grant shall be limited to a period not to exceed three months during the nonacademic portion of school year. 5. No senior investigator may have more than one student per year receiving a grant. 6. Only a brief progress report or summary will be required. Publication will be at the discretion of the senior investigator.

APPLICATION.—1. Application should be made in writing by the senior investigator to: Council on Foods and Nutrition, American Medical Association, 535 N. Dearborn St., Chicago 10, on or before Dec. 15, 1959. 2. Application shall include: (*a*) brief outline of study proposed, (*b*) assurance that adequate physical facilities are available, (*c*) identification of a qualified medical student and assurance of his availability.

COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Ferrous Fumarate (Ferrous Fumarate, Firon, Fumiron, Hemoton, Toleron).—The empirical formula of ferrous fumarate is $FeC_4H_2O_4$.

Actions and Uses.—Ferrous fumarate, is an anhydrous salt of a combination of ferrous iron and fumaric acid. It contains 33% iron by weight. Ferrous fumarate is employed clinically for the treatment of iron deficiency anemia. Available data, while limited, indicate that the drug is probably as effective for this purpose as other orally administered ferrous compounds. Thus, it may be expected to produce an adequate rise in hemoglobin levels (2 Gm. per 100 cc. in three weeks) and a satisfactory increase in hematocrit (5% or more in three weeks) in patients with microcytic, hypochromic anemias due to iron deficiency. Such anemias are commonly seen in infancy or pregnancy in which the demand for hemoglobin is increased or in situations in which there is a deficient intake of iron or an excessive loss of iron as in hemorrhage or heavy menstrual flow. If a satisfactory hematological response is not obtained after a therapeutic trial with the drug, medication should be stopped and other diagnostic measures begun. Failure to respond to hematinic agents may indicate that anemia is not due to iron deficiency, that complicating disease is interfering with the ability of the bone marrow to respond, that there is continuous active blood loss, or that there is impaired absorption of iron. Thus, it is important in all cases to search for the underlying cause of anemia.

The acute toxicity of ferrous fumarate in experimental animals is low. It is also well tolerated clinically, and there is some evidence to indicate that it may be superior to ferrous sulfate or ferrous gluconate in this respect. Thus, occasional patients will experience the gastrointestinal disturbances (anorexia, nausea, vomiting, cramping, diarrhea, constipation) typical of orally administered iron salts. These complaints are generally mild and tend to subside as therapy is continued. In some instances, ferrous fumarate may be used satisfactorily in patients unable to tolerate other orally given preparations. As with all drugs of this class, ferrous fumarate is contraindicated in the presence of peptic ulcer, regional enteritis, and ulcerative colitis. In patients with unusual sensitivity to orally given iron salts, preparations which are suitable for parenteral use should be employed. Also, when the cause of the anemia has been removed, a single dose of parenterally administered iron may be used to replace iron stores, in place of protracted oral therapy.

Dosage.—Ferrous fumarate is administered orally. Each 200 mg. of the drug is equivalent to about 65 mg. of elemental iron. For adults, the usual dose is 200 mg. three to four times daily. No data are available to permit dosage recommendations for infants and children.

Preparations.—tablets 200 mg. and 324 mg.

Year of introduction: 1957.

Mallinckrodt Chemical Works cooperated by furnishing scientific data to aid in the evaluation of ferrous fumarate.

Heparin Potassium (Clarin).—The potassium salt of heparin. The preparation is standardized in terms of the International Unit which represents the activity of 7.7 mcg. (0.0077 mg.) of heparin sodium standard.

Actions and Uses.—Heparin potassium is proposed for sublingual administration as an adjunct in the management of atherosclerosis by virtue of its effects on the physicochemical properties of the blood fats; it is not intended for use as an anticoagulant when given by this route. Heparin is a molecule of large size, and little absorption from the buccal mucous membrane is to be expected. At present the evidence is somewhat conflicting, but it indicates that amounts of the drug sufficient to approximate the action of small doses of parenterally injected heparin sodium on the physicochemical state of the blood fats are often, but not always, absorbed from beneath the tongue. Thus, the potassium salt, when given by the sublingual route, may cause the same changes in the physicochemical state of blood lipids as has been previously described for injections of the sodium salt. (See the monograph on heparin sodium, U. S. P., in New and Nonofficial Drugs.) However, there is as yet no convincing objective evidence that heparin, given sublingually, either prevents or ameliorates any manifestation of cardiovascular disease. Hence, the use of heparin potassium in the hope of ameliorating the progress of atherosclerosis must be considered experimental.

In the doses usually employed, heparin potassium has shown no demonstrable effect on clotting time and is believed to be relatively safe for use, from the standpoint of possible adverse effects on blood coagulation.

Dosage.—Heparin potassium is administered sublingually. The proposed dose is 1,500 International Units three times a day given after meals.

Preparations.—tablets (sublingual) 1,500 International Units.

Year of introduction: 1958.

Thos. Lemming & Co., Inc., cooperated by furnishing scientific data to aid in the evaluation of heparin potassium.

Penicillinase (Neutrapen).—A specially purified enzyme preparation obtained by fermentation from cultures of a strain of Bacillus cereus. A unit of penicillinase is defined as that amount which, in vitro, inactivates one unit of penicillin per minute at 25 C at a pH of 7.0.

Actions.—Penicillinase is an enzyme preparation proposed for use in the treatment of reactions to penicillin. The enzyme catalyzes the hydrolysis of the β-lactam ring of penicillin; the resulting product is penicilloic acid, which is biologically and, presumably, antigenically inactive. Penicillinase is produced not only by B. cereus, but also by certain strains of Escherichia coli, many strains of staphylococci, and by a large variety of other bacteria. It probably contributes significantly to the resistance of some, but not all, penicillin-insensitive micro-organisms.

Within a short time after injection of penicillinase, penicillin can no longer be detected in the blood, even when blood levels prior to this injection are quite high. Experimental studies in rabbits have shown that, when 5,000 units of penicillinase were injected simultaneously with 100,000 units of either potassium penicillin G or procaine penicillin G, blood levels of penicillin returned to zero within one hour after injection. When the dose of penicillinase was increased to 10,000 units, no penicillin was detectable at any time after injection. The duration of action of a single injection of penicillinase was found to be about four days. Similar results have been reported in guinea pigs. In human patients who had received 800,000 units of procaine penicillin G, a single injection of 100,000 to 800,000 units of penicillinase was found to completely eliminate penicillin from the blood within one hour. No penicillin could be detected in the blood for periods of four to seven days,despite the fact that injections of penicillin were continued twice daily.

Although penicillinase has had only limited clinical trial in the treatment of reactions to penicillin, early reports, based on uncritical studies, are favorable. Some response to treatment may occur within six hours but usually is seen only after one to four days. The various manifestations of delayed reactions to penicillin, including skin eruptions, urticaria, arthralgia, asthma, and fever, are reported to respond favorably to the enzyme. Reactions to procaine penicillin G are said to clear as quickly as those to the longer-acting benzathine penicillin G. Results are best when the penicillinase is administered within 24 hours after the reaction has begun.

Uses.—Penicillinase may be employed for the treatment of slowly developing or delayed penicillin reactions. Adjunctive use of more rapidly acting drugs may prove necessary or advisable, however. It should also be remembered that a considerable period of time will be required for recovery from physical changes associated with penicillin reactions, even after all traces of penicillin are removed from the body.

Anaphylactic reactions to penicillin should first be controlled by epinephrine and other rapidly acting agents; penicillinase may then be given to eliminate the circulating antigen, if desired. Reliance on penicillinase alone in such reactions is contraindicated, since effects of the enzyme are evident only after several hours.

The use of penicillinase as a diagnostic agent to distinguish between penicillin reactions and other syndromes must be regarded as experimental. Similarly, its possible value in preventing reactions in patients who are known to be sensitive to penicillin and who are given injections of vaccines or other penicillin-containing products has not been established. *Neither of these uses (diagnostic or prophylactic) is recommended for routine application at the present time.*

The use of penicillinase is an interesting approach to the treatment of penicillin reactions. Destruction of the causative agent rather than mere suppression of symptoms is certainly logical and desirable on theoretical grounds. At the present time, however, the efficacy of penicillinase has not been established. Recovery from penicillin reactions often occurs spontaneously within a few days, even when no treatment is administered. For this reason, assessment of the value of any agent used for treatment of these reactions requires the most carefully designed clinical trials. Such trials of penicillinase have not yet been done; no double-blind study has been reported.

Side-effects.—Experimental animal studies indicate that penicillinase has a remarkably low acute toxicity. Doses as high as 10,000,000 units per kilogram of body weight given intramuscularly are well tolerated. Chronic toxicity studies revealed no adverse effects from daily injections for a period of six weeks. However, since penicillinase is an enzyme and, therefore, almost certainly a protein, it must be regarded as an antigen. In addition, all the other dangers attending the injection of a foreign protein will probably be noted. Indeed, several severe reactions which closely followed the injection of penicillinase in human patients have already been reported. The symptoms of these reactions suggested an acute anaphylactoid response, although none of the patients had previously received penicillinase. Less serious reactions that have been observed in clinical usage include local pain at the site of injection, weakness, malaise, a morbilliform rash, and a mild, self-limited febrile reaction.

Dosage.—Penicillinase is administered by deep intramuscular injection. It should be freshly dissolved in sterile distilled water just prior to use. The concentration of penicillinase in the solution should be 400,000 units per cubic centimeter. The proposed dose for adults is 800,000 units (2 cc. of such solution). The dose may be repeated at intervals of three to seven days if necessary. It is claimed that two injections are usually sufficient to afford permanent relief from the symptoms of a single reaction.

Preparations.—powder (injection) 800,000 units.

Year of introduction: 1958.

SchenLabs Pharmaceuticals, Inc., cooperated by furnishing scientific data to aid in the evaluation of penicillinase.

STRESS.—In biology and medicine the term stress is of comparatively recent introduction and has been variously applied to external stimuli as well as their effects on the organism. . . . In general medicine and psychiatry the term stress is commonly used to denote various psychosocial situations which tend to produce disorganization of behavior, including physical and mental illnesses. Responses of different individuals to potentially stressful psychosocial situations show considerable variation. The response may be apt and adaptive or it may be inept or maladaptive, the latter sometimes taking the form of physical or mental illness. The precise relationships between the psychosocial situations which are potentially stressful and their effects on the organism on the one hand, and the various stress or agents described by Selye and their effects on the organism on the other, require further research for their elucidation. A convenient definition of stress would be any stimulus or change in the external or internal environment which disturbs homeostasis and which, under certain conditions, can result in illness. The terms stress and stressor are really abstractions and are only meaningful in relation to their effects on the organism and it might be better to use stress adjectivally. . . . to the three distinct processes involved in reactions to stress, namely: (1) The forces, stimuli, changes, conditions or situations which are stressful. (2) The processes whereby (1) produce their effects on the organism. (3) The changes in the organism resulting from (1), including behavioural, emotional, physiological, biochemical and structural changes. —L. Rees, M.D., The Role of Stress in the Aetiology of Psychosomatic Disorders, *Proceedings of the Royal Society of Medicine,* April, 1959.

COMMITTEE ON REHABILITATION

The following report is the first in a series of articles which have been authorized for publication by the Committee. This series deals with various aspects of rehabilitation which are of interest to physicians.

RALPH E. DE FOREST, M.D., *Secretary.*

THE STATE-FEDERAL PROGRAM OF VOCATIONAL REHABILITATION

Since 1921 the state governments and the federal government have jointly operated a program of rehabilitation services designed to restore handicapped men and women to activity and to employment. During the year ended June 30, 1958, almost 75,000 disabled persons received services and were placed in useful employment. About 18,000 more were provided with services that prepared them for employment but at the end of the fiscal year had not found jobs. About 159,000 persons were in the process of rehabilitation at the end of the period. The program is in operation in all states, the District of Columbia, Puerto Rico, the Virgin Islands, and Guam.

Medical services have been an integral part of the program since 1943, and private practitioners and county and state medical societies and hospitals have been active both in the provision of services and in guidance of the program. About one-third of referrals of disabled persons to state rehabilitation agencies come from physicians, hospitals, and welfare agencies. Since the physician is usually one of the first to see an injured person, and in many cases has close knowledge of circumstances surrounding individual disabilities that arise out of disease or congenital difficulties, it is widely believed that there is opportunity for a larger number of referrals from physicians if more of them are fully aware of the rehabilitation services available to those disabled persons with employment potentialities. A survey just completed among physicians selected from a county medical society in one of our more populous areas points up this fact. (This survey was one of the research projects aided by a grant from the Office of Vocational Rehabilitation.) The physicians who were interviewed were from those specialty groups most likely to see patients who might need, and be eligible for, rehabilitation services offered by the state rehabilitation agency. It was found that, as a whole, these physicians had relatively little knowledge about their state rehabilitation agency. One-third of them did not know that the agency existed; another one-third knew little more about the agency than that it did exist. Only 5.5% knew some of the general eligibility requirements for handicapped persons to receive services, and about half of them were physicians in institutional practice.

The physicians who were aware of the public rehabilitation program gave many reasons for the lack of prompt referrals of disabled persons to the state rehabilitation agency. According to the report, some of them expressed regret for lack of action. The total effect of this survey was to indicate a positive necessity for wider knowledge of the public rehabilitation program, and of the emphasis that is placed on a proper balance in individual cases, between medical and vocational orientation.

Integration of medical services into the program began with amendments to vocational rehabilitation legislation after the outbreak of World War II, when there arose the acute need for civilian manpower. In this labor shortage the nation made its first, though halting, efforts to bring qualified disabled workers into the labor force. There was a prior factor that had led to establishment of a civilian rehabilitation program—the consideration of what was being done to rehabilitate the veterans of World War I and the recognizable need for a concurrent program for disabled civilians.

Congress enacted the first rehabilitation legislation in 1920. The services provided in this early program were limited in range, compared with today's program. They included principally special assistance in job training, counseling and guidance, provision of artificial limbs and other appliances, and placement in a suitable job. No provision was made for federal participation in any sort of medical or restorative services to reduce or eliminate the disability itself, although a few states undertook a limited amount of such service on their own initiative.

During the 1920's and 1930's, more and more states joined this cooperative state-federal program, so that by 1938 all of the 48 states were participating.

With the outbreak of World War II, one of the obvious steps to reduce manpower shortages was to make greater use of handicapped workers. In 1943

The members of the Committee on Rehabilitation of the American Medical Association are Drs. Frank H. Krusen, Rochester, Minn., Chairman; Walter H. Baer, Peoria, Ill.; Guy A. Caldwell, New Orleans; Oscar A. Sander, Milwaukee; and Hoyt B. Woolley, Idaho Falls, Idaho.

Congress passed Public Law 113, 78th Congress, known as the Barden-LaFollette act. This act expanded the scope of services and authorized for the first time the provision of (1) medical services including surgery, hospitalization, and other treatment to eliminate or reduce the disability itself, (2) services to individuals who had suffered from psychiatric illnesses, and (3) vocational rehabilitation services for the blind.

In August, 1954, major amendments were made to the act through Public Law 565, 83rd Congress. This act, while continuing the basic provisions for services to handicapped people through the state vocational rehabilitation agencies, introduced a number of important changes. 1. A new system of federal-state financing for the basic program of vocational rehabilitation services was introduced. 2. A new system of extension and improvement grants to state agencies was authorized, to give encouragement and financial aid to the states to develop new aspects of rehabilitation and to extend services to disability groups and geographical areas which heretofore had been inadequately served. 3. Federal grant funds were authorized to encourage and support research into better rehabilitation methods and to conduct demonstration projects which would be useful in spreading new knowledge to communities throughout the country. These grants are made primarily to universities and other institutions having research talent and facilities for advancing rehabilitation knowledge, as well as nonprofit voluntary groups capable of conducting such research and demonstration. 4. Grants were authorized to universities and other teaching institutions to stimulate and support the training of more professional personnel for rehabilitation services. Grants for traineeships for students are made in a block grant to the university, which then selects the students considered most qualified for traineeship awards. Training grants are also used to help support specialized short-term courses to provide "brush-up" and other intensive training in specialized fields of rehabilitation. 5. Provisions were included in the act to give preference to blind persons in the operation of vending stands on federal property. 6. To stimulate the employment phase of vocational rehabilitation, the act required that each state-federal employment service office designate at least one staff member to provide special job counseling and placement for handicapped persons. It also authorized a larger annual appropriation for the work of the President's Committee on Employment of the Physically Handicapped. 7. The use of federal funds (in combination with those of states and voluntary agencies) was authorized to enlarge or alter rehabilitation centers. 8. The establishment of vocational rehabilitation agencies within local units of government (cities or counties) was authorized for the first time with federal financial participation, provided the local unit was under the general direction of the state agency.

In order to be eligible for any of the services offered in vocational rehabilitation, an individual must (1) have a disability which substantially interferes with suitable employment, (2) have a reasonable chance to become suitably employed after services are provided, and (3) be of, or near, working age.

The medical staff of the state rehabilitation agency has specific responsibility in these determinations. An applicant talks with a counselor, either in an office of the rehabilitation agency or in the applicant's home. The applicant is asked to furnish any available medical data concerning his disability. In its absence, the agency will provide for an examination, and, if the services of a specialist are required, the agency will bear the cost.

If an applicant is accepted, a program of rehabilitation services based on individual need will be formulated to include these measures as required: (1) medical diagnosis to learn more about the nature and degree of disability and to help to determine the program of rehabilitation services, the need for additional medical services, and the individual's work capacities; (2) provision of artificial limbs or other prosthetic appliances; (3) individual counseling and guidance, including psychological testing, to help select and attain a vocational objective; (4) training, including occupational training and adjustment training for the blind; (5) maintenance and transportation during treatment, training, or any other phase of the actual rehabilitation process; (6) tools, equipment, licenses, or initial stocks and supplies if these are necessary to give the rehabilitated individual a fair start; (7) placement in a job commensurate with the individual's physical and mental capacities; and (8) follow-up to ensure that the rehabilitated person is successful and that both he and his employer are satisfied.

In the last few years, Congress has passed several pieces of legislation which, while primarily involving other federal agency programs, have important involvements for vocational rehabilitation. The 1954 Amendments to the Hospital Survey and Construction Act of 1947 (the Hill-Burton act) authorized federal grants-in-aid to help build rehabilitation facilities. The general administrative machinery of the Hill-Burton program is used, with the surgeon general of the Public Health Service and the director of Vocational Rehabilitation having joint authority for approval of applications for grants for rehabilitation facilities.

During the same year, the Congress amended the Social Security Act to "freeze" the retirement benefits of workers covered by the act who became disabled. The purpose was to ensure that an eligible worker who became disabled before reaching age 65 did not have his retirement income reduced because of any years during which he was unable to contribute to the Old Age and Survivors' Insurance trust fund because of disability. To carry out this new provision, Congress indicated that the state vocational rehabilitation agency was its preference for making a determination as to whether the applicant was, in fact, disabled and unable to work under the provisions of this law. At present, the state vocational rehabilitation agencies perform this function in all but 4 of the 54 states and territories.

In 1956, the Social Security Act was further amended to provide that disabled workers aged 50 or over and eligible for Old Age and Survivors' Insurance benefits, who were unable to work because of their disability might receive cash retirement benefits six months after onset of the disability. Again the state vocational rehabilitation agencies were designated as the preferred agency to make the determination of disability. Specific provisions were made for referring all such applicants to the state rehabilitation agencies in the increasing effort to restore all possible disabled workers to gainful activity. Also eligible to receive cash benefits were disabled and dependent children of retired or deceased workers entitled to old-age benefits, provided the disability existed before the age of 18 years.

For the fiscal year ending June 30, 1959, the federal appropriation for basic vocational rehabilitation services totals $45,500,000. For the same period, the states have matching funds available totaling about $27,900,000.

The sum of $4,600,000 is available for the research and demonstration program in fiscal 1959, making a total of around 11 million dollars that will have been expended or obligated by the end of the period. Some 230 projects have been completed, are in operation, or have been approved for operation since the start of the program. They range through most aspects of rehabilitation, and a great many of them have to do with medical investigations in the problems of disability and rehabilitation.

Sponsors of research projects make application directly to the federal Office of Vocational Rehabilitation, where the National Advisory Council on Vocational Rehabilitation reviews each application and recommends action. As of Jan. 1, 1959, two nationally known physicians were members of the advisory council.

Each application for a research grant competes with other applications on the basis of merit. The sponsor of the research project is required by law to bear a share of the total cost; however, no fixed ratio between federal funds and sponsor is specified, and the actual financial participation is determined project by project, depending on the nature of the work to be done. In the projects initiated so far, the grantee share has averaged around one-third of the total cost.

The training grant program, to prepare more professional personnel in rehabilitation, increased from $2,950,000 in fiscal 1957 to $4,400,000 in 1958, including almost 2 million dollars to colleges, universities, and other institutions to strengthen their instructional resources in rehabilitation medicine and related subjects. Twenty-five medical schools have received teaching grants to expand instruction in rehabilitation principles and practices to undergraduate students. Also, by the end of the last fiscal year, 189 physicians had received from the Office of Vocational Rehabilitation traineeships for their support during their residency training in physical medicine and rehabilitation, and 142 physicians are now in long-term residency training programs, with financial assistance from this same agency.

The new emphasis of the program has brought about close relationships between the Office of Vocational Rehabilitation and state agencies with medical societies, for counsel and development of policy; with colleges of medicine for the development of physical medicine and rehabilitation, and for the training of medical students and other groups in rehabilitation principles; with engineering schools and medical schools for the development of prostheses; with research groups for inquiry into new medical phases of rehabilitation; with voluntary groups interested in the medical phases of specific disabilities; and with community organizations interested in establishing or expanding rehabilitation facilities.

The medical profession is represented in the Office of Vocational Rehabilitation by the chief medical officer and a medical consultant. There are positions for medical consultants in the nine regional offices of this agency, of which only three are filled at present due to the difficulty of recruiting adequately trained physicians in the federal service. The state vocational rehabilitation agencies have state and district medical consultants. Counties and municipalities and voluntary groups engaged in rehabilitation activities seek the counsel of medical societies and groups on their own special problems, so that the whole program of rehabilitation, public and private, can be soundly based on the medical orientation and cooperative working relationships that are so vital to the hopes of the disabled.

This report was prepared in cooperation with the Office of Vocational Rehabilitation, Miss Mary Switzer, Director, U. S. Department of Health, Education, and Welfare.

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NEWER CONCEPTS OF JAUNDICE

SINCE the discovery by Ehrlich in 1883 of a color reaction which permits the estimation of bilirubin, quantitation of this substance has played an important role in diagnosis and treatment of numerous diseases. The usefulness of this method was increased by the development of the van den Bergh method for quantitative estimation of bilirubin and for qualitative discrimination of the etiology of jaundice. Obstructive jaundice is accompanied by an increase in "direct bilirubin" while hemolytic jaundice is characterized by an elevation of "indirect bilirubin." Direct bilirubin refers to the prompt reaction in serum after addition of appropriate reagents while indirect bilirubin signifies the reaction dependent on the additional presence of alcohol.

Although this empirical distinction has been of great value in clinical medicine, understanding of these phenomena eluded investigators until recently. The discovery of the nature of direct and indirect bilirubin coupled with the elucidation of the mechanism of uronide formation has made possible a new order of comprehension of many clinical and biological phenomena.

The finding by Schmid[1] and Billing and Lathe[2] that direct bilirubin contains glucuronic acid whereas indirect bilirubin lacks glucuronic acid offered for the first time a satisfactory explanation of the difference in the van den Bergh reaction in obstructive and in hemolytic jaundice. Bilirubin, like many other substances, is detoxified in the liver by conjugation with glucuronic acid. In obstructive jaundice conjugated bilirubin results in the direct reaction while the large increase of unconjugated bilirubin in hemolytic jaundice results in an increase in the indirect reaction.

Simultaneous with these discoveries has been a series of advances in the understanding of uronide formation. Dutton and Storey[3] demonstrated that the synthesis of uronides in the liver is dependent on the presence of two factors, a heart-stable coenzyme and a heart-labile enzyme. The coenzyme was identified as uridine diphosphoglucuronic acid (UDPGA). This coenzyme belongs to a family of uridine compounds which are involved in a variety of biosynthetic reactions concerned with the mechanism for the donation of monosaccharide units. In the case of uronide formation the reaction may be portrayed as follows:

$$\text{UDPGA} + \text{acceptor} \rightarrow \text{Uronide} + \text{UDP}$$

This reaction occurs in the formation of uronides of many substances including phenols, alcohols, and amies. Included are drgus, e. g., salicylates and physiological compounds such as the steroid hormones.

In the case of bilirubin metabolism the reaction may be more specifically designated as follows[4]:

$$\text{UDPGA} + \underset{\text{(indirect bilirubin)}}{\text{bilirubin}} \rightarrow \underset{\text{(direct bilirubin)}}{\text{bilirubin glucuronide}} + \text{UDP}$$

The enzyme which catalyzes this reaction is a transferase and has been demonstrated in the liver of a number of species.

Studies on the distribution of this enzyme already have had important implications in clinical medicine. Lathe and Walker[5] discovered that the liver in newborn infants is relatively deficient in the transferase enzyme. This results in a diminution of bilirubin conjugation with a consequent increase of indirect bilirubin in the human neonate. A deficiency in the transferase enzyme has also been demonstrated in fetal tissues of other species. These findings probably explain the frequency of jaundice in the premature infant. It has been suspected that kernicterus results from indirect rather than direct bilirubin. The occurrence of kernicterus in premature infants as well as in erythroblastosis fetalis now becomes understandable.

A deficiency in the enzyme, transferase, appears responsible for the heritable disease, congenital nonhemolytic jaundice with kernicterus—a disease characterized by kernicterus in the presence of an elevated level of indirect bilirubin.[6] A similar defect appears to be present in Gilbert's disease, familial nonhemolytic jaundice.[7] Although clinically distinct from congenital nonhemolytic jaundice with kernicterus, the difference in biochemical lesion in the two syndromes is not yet apparent. It is interesting to note that a similar deficiency of the transferase enzyme has been demonstrated in a strain of jaundiced rats.[5]

The discovery of the chemical nature of direct and indirect bilirubin and the mechanism of unronide formation already has led to rapid advances in the understanding of disturbances of bilirubin metabolism.

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ORGANIZATION SECTION

THE SCIENTIFIC PROGRAM

Miami Beach, June 13-17, 1960

The Council on Scientific Assembly is presently considering scientific subjects for presentation in the Scientific Assembly at the Annual Meeting of the American Medical Association in Miami Beach, Fla., June 13-17, 1960. The lecture program of the Annual Meeting is developed by the secretaries of each of the 21 sections of the Scientific Assembly. In order to coordinate all scientific programs (lectures, movies, television, and the scientific exhibits), the titles of proposed papers should be submitted to the section secretaries not later than Dec. 15, 1959.

Since the program is now in the formative stages, all medical scientists who are considering the presentation of scientific papers before the medical profession at the Annual Meeting should communicate at the earliest possible date with the secretary of the section before which he wishes to present his subject. It is emphasized that the completed paper need not be ready by Dec. 15, 1959. In many instances, the material to be presented at the June meeting represents research that is currently being undertaken and cannot be completed until a short time before the meeting.

The Scientific Exhibit is arranged by the Council on Scientific Assembly in cooperation with the representatives from the sections to the Scientific Exhibit. Application blanks for space in the Scientific Exhibit may be obtained from the section representative or the Secretary of the Council on Scientific Assembly, American Medical Association, 535 N. Dearborn St., Chicago 10. All applications must be submitted by Jan. 10, 1960. Due to the large number of applications received in the past and in view of the limited space available, applicants are urged to submit their applications as early as possible.

Application blanks for presentation of films on the motion picture program may be obtained from Mr. Ralph Creer, Director, Medical Motion Pictures and Television Department, Communications Division, American Medical Association, 535 N. Dearborn St., Chicago 10. The closing date for acceptance of these applications is Jan. 10, 1960. Since films are previewed prior to acceptance, applications for time on this program should be made as early as possible.

The names and addresses of the Section Secretaries and Representatives to the Scientific Exhibit are:

Anesthesiology

Secretary—Vincent J. Collins, M.D., New York University-Bellevue Medical Center, 550 First Ave., New York 16.

Exhibit Representative—Edwin L. Rushia, M.D., University Hospital, Augusta, Ga.

Dermatology

Secretary—Edward P. Cawley, M.D., University of Virginia Hospital, Charlottesville, Va.

Exhibit Representative—Stanley E. Huff, M.D., 636 Church St., Evanston, Ill.

Diseases of the Chest

Secretary—Burgess L. Gordon, M.D., The Lovelace Foundation, 4800 Gibson Blvd. S. E., Albuquerque, N. Mex.

Exhibit Representative—Edwin Rayner Levine, M.D., 111 N. Wabash Ave., Chicago 2.

Experimental Medicine and Therapeutics

Secretary—Samuel P. Martin, M.D., University of Florida School of Medicine, Gainesville, Fla.

Exhibit [illegible] F. Ross, M.D., Departmen[illegible] and Radiation Biology, University of California School of Medicine, Los Angeles 24.

Gastroenterology and Proctology

Secretary—Gordon McHardy, M.D., 3636 St. Charles Ave., New Orleans 15.

Exhibit Representatives—Willard Bernhoft, M.D., 2900 Main St., Buffalo 14, and Thomas E. Machella, M.D., 3400 Spruce St., Philadelphia 4.

General Practice

Secretary—Eugene I. Baumgartner, M.D., 25 Alder St., Oakland, Md.

Exhibit Representative—I. Phillips Frohman, M.D., 2924 Nichols Ave., S. E., Washington 20, D. C.

Internal Medicine

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Exhibit Representative—Henry T. Ricketts, M.D., 950 E. 59th St., Chicago 37.

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Secretary—Walter E. Heck, M.D., Stanford University Hospital, San Francisco 15.

Exhibit Representative—Walter H. Maloney, M.D., University Hospitals, 2065 Adelbert Rd., Cleveland 6.

Military Medicine

Secretary—James T. McGibony, M.D. (Colonel, M. C., U. S. Army), Medical Plans & Operations Division, Office of the Surgeon General, Department of Army, Washington 25, D. C.

Exhibit Representative—Frank M. Townsend, M.D. (Colonel, M. C., U. S. A. F.), Armed Forces Institute of Pathology, Washington 25, D. C.

Nervous and Mental Diseases

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Exhibit Representative—F. Thomas Mitchell, M.D., LeBonheur Children's Hospital, 848 Adams at Dunlap, Memphis 5, Tenn.

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Exhibit Representative—Ralph E. Worden, M.D., University of California Medical Center, Los Angeles 24.

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Secretary—Lemuel C. McGee, M.D., 900 N. Market St., Wilmington 99, Del.

Exhibit Representative—Paul A. Davis, M.D., 633 E. Market St., Akron 4, Ohio.

Radiology

Secretary—Traian Leucutia, M.D., Harper Hospital, Detroit 1.

Exhibit Representative—Richard H. Chamberlain, M.D., 3400 Spruce St., Philadelphia 4.

Surgery, General and Abdominal

Secretary—Edwin H. Ellison, M.D., 8700 W. Wisconsin Ave., Milwaukee 13.

Exhibit Representative—Julian Johnson, M.D., 3400 Spruce St., Philadelphia 4.

Urology

Secretary—Edward H. Ray, M.D., 2101 Nicholasville Rd., Lexington, Ky.

Exhibit Representative—E. F. Poutasse, M.D., Cleveland Clinic, 2020 E. 93d St., Cleveland.

NOMINATIONS FOR GENERAL PRACTITIONER AWARD

Nominations for the annual General Practitioner of the Year award must be submitted by Oct. 26. The winner will be announced Dec. 1 at the opening meeting of the House of Delegates at the Clinical Meeting in Dallas. The nominations are made by state medical societies and the award winner is chosen by a committee appointed by the chairman of the A. M. A.'s Board of Trustees. Societies should mail their nominations to Dr. F. J. L. Blasingame, Executive Vice-president, A. M. A. 535 N. Dearborn, Chicago 10.

COUNCIL ON MEDICAL SERVICE

AHA ABSTRACTING SERVICE

The American Hospital Association, in an attempt to keep hospital administrators and those in the allied professions in touch with the rapidly changing medical scene, started a new abstracting service on Oct. 1, 1959. The service will, of course, be primarily geared to hospital needs, but a wide scope is envisaged for the service. Material on hospital function, design, construction, and financing will be abstracted, as well as metropolitan surveys of facilities, services, and needs, legislative developments, and trends in medicine and the socioeconomic field.

Dr. Edwin L. Crosby, director of the association, reports that there have been a number of requests for such a service. "The hospital field is alive with change. . . . The twin pressures of expanded medical research and rising costs of hospital operation are causing the whole hospital field to make an almost constant reevaluation of programs." The abstracting service will sift the flood of material, in articles, books, pamphlets, reports, and journals, to aid those in the hospital field to make such reevaluations.

The abstracts will be published as sets of 4 in. by 6 in. cards, issued six times a year. Each card will contain one abstract, indexed by subject, giving complete data as to source for those who wish to consult the original. Price of a one-year subscription is $10. The filing-card method of publication will facilitate grouping abstracts by subject for future reference.

Although the service is designed primarily to fill the needs of those in the hospital field—administrators, trustees, architects, and consultants—it may also be of considerable help to medical organizations and individual physicians interested in hospital-medical trends. Detailed information on the service is available from Hospital Planning Abstract Service, American Hospital Association, 840 N. Lake Shore Dr., Chicago 11.

DEPARTMENT OF ECONOMIC RESEARCH

VOLUNTARY HEALTH INSURANCE PAYMENTS FOR SHORT-TERM GENERAL HOSPITAL STAYS OF AGED PERSONS

Walter Polner, Ph.D.

By the summer of 1958, 43% of all persons 65 years of age and over, or 6,600,000 persons, had purchased voluntary health insurance to help pay for the costs of potential hospital, surgical, or medical care.[1] With the extension of various programs of health insurance among persons 65 years of age and over, there is wide interest in reappraising how these programs are meeting the charges for hospital care. The purpose of this paper is to appraise current methods being used to ascertain the extent of the hospital costs of the aged covered by voluntary health insurance and to suggest alternative methods.

While there has been a great deal of discussion concerning the hospital payment "problems" of the aged, the extent of the payment of hospital bills by voluntary health insurance has received only slight treatment, due to the research problems involved. These available data, while useful as trends, have little more than sketched the impact of voluntary health insurance on meeting the short-term general hospital charges of these aged persons.

Why should this be? Part of the explanation for the lack of accurate information on voluntary health insurance payments for hospital care may be due to (*a*) the magnitude of the increase in voluntary health insurance since 1951 when "at most 15%,"[2] or 1,800,000 persons 65 years of age and over had voluntary health insurance, (*b*) the increase in the scope of benefits provided by voluntary health insurance, and (*c*) lack of information on the hospital charges to be properly paid for by voluntary health insurance.

Medical Care Costs Method

What methods presently are being used to measure voluntary health insurance payments for hospital stays of aged persons? The most comprehensive recent study has been that of the Bureau of Old Age and Survivors Insurance (B/OASI) of the Social Security Administration among their beneficiaries in 1957.[3] The Bureau attempted to survey a selected sample of 1,849 couples and 2,280 individual persons to ascertain the "medical care costs" of the beneficiaries and the amount of these costs that was being covered by any type of voluntary health insurance. Since the survey was interested in all medical care costs, it included the following items: psychiatric care, outpatient clinic use, osteopathic services, chiropractic services, faith-healing services, chiropodist services, nursing home care, purchase of appliances (such as eye glasses and braces), the purchase of prescription and proprietary drugs, the hiring of extra household help needed due to illness, as well as the actual payment made to the hospital and physician. Due to the broad nature of the interest of the study, in its attempt to gather total medical care costs, the study concluded that "relatively few—14% of the couples and 9% of the nonmarried beneficiaries—had any of their [total medical care] expenses covered by insurance."[4]

Further analysis of the data shows that 79% of all OASDI beneficiary couples and 85% of all OASDI nonmarried beneficiaries surveyed did not enter a hospital during the survey period. Therefore, since most of the present voluntary health insurance is hospital-oriented, these resulting data were to be expected. The payments for proprietary drugs, for osteopathic services, chiropodist services, eye glasses, eye glass frames, and dental care, although they all may be necessary medical care services, would normally not be covered by most types of voluntary health insurance. It is one matter to decide whether they should be covered; it is another consideration entirely to ascertain how well the voluntary health insurance does cover the areas of hospital care for which it attempts to provide payment. An analysis of these data to determine the number that may have had voluntary health insurance to help pay for a hospital stay indicates that the majority of those persons who did use the hospital could have received aid in paying for their hospital care from voluntary health insurance.

Of all the total beneficiary couples surveyed (1,849 or 100%) (table 1), only 14% (259) had any aid from voluntary health insurance for payment of their expenditures for medical care. The total number of couples who actually did use the hospital was 373 (20%). While only 43% of the total OASDI population has voluntary health insurance, approximately 65% of those couples who did use the hospital could have obtained aid in paying for hospital charges. Due to the administrative needs of the research design the OASDI survey did not separate the hospital bill, in-hospital surgical bill, and in-hospital medical bill which were paid for by voluntary health insurance. Information was provided only on the total medical care charges, in and out of the hospital, for the 20% who actually used the hospital. The data in table 1 suggest that more than 14% of the group using the hospital were aided in payment of their hospital bills by voluntary health insurance.

Hospital Charges

A more important question is whether the hospital charges, taken separately, could give a better idea of the extent of aid provided by voluntary health insurance in the payment of hospital bills. Since the total medical care expenditures for the aged do not give a realistic appraisal of what proportion of the hospital cost of the aged person the voluntary health insurance mechanisms are providing, would information concentrated primarily on hospital charges give any better indication?

TABLE 1.—*Number of Aged Couples and Nonmarried Beneficiaries of OASDI Hospitalized and Medical Costs Incurred During 1957**

Total Medical Cost, in Dollars	OASDI Beneficiary Couples	OASDI Beneficiary Couples Hospitalized, No.			OASDI Nonmarried Beneficiaries	OASDI Nonmarried Beneficiaries Hospitalized, No.		
		Total	General Hospital	Long-Stay Institution		Total	General Hospital	Long-Stay Institution
None	52	..	..	..	189	..	..	..
1- 99	523	3	3	..	961	8	8	..
100-199	318	13	13	..	385	32	32	..
200-299	235	22	22	..	194	27	26	1
300-399	161	34	33	1	87	21	19	2
400-499	102	35	34	1	59	24	22	2
500-599	76	34	34	..	21	12	12	..
600-799	65	36	35	1	39	27	25	2
800-999	42	31	31	..	23	19	12	7
1,000-or more	122	108	102	6	98	83	50	33
Some "free care"	107	47	37	10	178	81	62	19
Unknown	46	30	29	1	43	24	21	3
Total	1,849	393	373	20	2,280	358	289	69

* Source: Social Security Bulletin 22:3-5 (April) 1959.

Normal Method of Measuring Payments

The normal method used to determine the portion of the hospital bill paid by voluntary health insurance is total voluntary health insurance hospital payment (TVHIHP) divided by total hospital bill (THB), $[\frac{\text{TVHIHP}}{\text{THB}}]$. Adjustment in the THB is made to eliminate payment by public revenues either in publicly controlled hospitals or for the purchase of services in privately controlled hospitals under such programs as Medicare or public assistance. In 1957, by using this general method, the Social Security Administration estimated for the entire population that $2,302,607,000, or 57.3%, of the United States' short-term general hospital bill was paid for by voluntary health insurance (table 2). Research in Michigan by the Michigan Blue Cross, however, provides information that approximately 90% of the hospital bill of the aged person covered by that plan was paid for by the plan.[5] Other studies also show that more than 50% of the hospital bill was covered by a voluntary health insurance mechanism (table 3).

Alternative Method of Measuring Payments

Since there are different statistics arising from these studies, some alternative method is called for in determining the extent of payment of hospital bills of the aged. If we assume that information is desired on the short-term general hospital stay by the aged, the basic formula of the Social Security Administration should be modified by making adjustments in both the TVHIHP and the THB statistics.

The TVHIHP should be adjusted to take into account the fact that although the aged are purchasing voluntary health insurance to a greater extent, some have other needs and desires that have greater priority. Therefore some of the aged, when they are offered voluntary health insurance, may have a tendency to purchase a less extensive type of voluntary health insurance with the conscious knowledge that this will provide only partial coverage of charges in the hospital. At a time when a person can purchase comprehensive plans with 120 days of hospital benefits from voluntary health insurance organizations, the primary desires of the person tend to limit his purchase to a 30-day or 60-day hospital plan. Persons can purchase plans that will pay up to $20 to $25 a day. They may desire, however, to use their income in other ways, and, therefore, they may purchase less extensive plans.

When only a certain percentage of hospital charges is paid for by voluntary health insurance, is this a weakness of the voluntary health insurance or the result of personal allocation of income among competing goals? Recent surveys of Health Information Foundation–National Opinion Research Center have indicated that aged persons were a little less interested in the need for voluntary health insurance than the younger population.[6] In an attempt to determine the extent of voluntary health insurance payments for hospital charges of the aged, adjustment must be made for the desire of the aged person not to purchase the best possible plan available. This is not a failure or a weakness of the voluntary health insurance; it is the desire of the individual person to make his own choices.

Table 2.—*Private Expenditures for Medical Care and Hospital Services Only, and Percentage Accounted for by Voluntary Health Insurance, 1948-1957**

	Total Medical Care Expenditures		Hospital Services Only†	
Year	Total Amount, Million Dollars	Paid by Insurance Coverage, %	Total Amount, Million Dollars‡	Paid by Insurance Coverage, %
1948	7,369	8.2	1,667	27.3
1950	8,320	11.9	2,100	32.4
1952	9,641	16.6	2,534	42.4
1954	11,156	19.5	3,056	47.2
1956	13,488	22.4	3,765	53.7
1957	14,392	24.1	4,019	57.3

* Source: Brewster, Agnes W.: Voluntary Health Insurance and Medical Care Expenditures: Ten-Year Review, Social Security Bulletin, 21:13 (Dec.) 1958.

† With expense to obtain insurance excluded.

‡ Expenditures include outpatient services provided by hospitals. Insurance benefits are applicable to such services when service is given in an emergency.

The THB statistic should also be adjusted to take into account the following items:

1. That portion of the hospital bill that normally is not expected to be paid for by voluntary health insurance. At the present time, some items to be excluded are the differences between the charges for a semiprivate room and a private room and other personal elective services, such as phone calls, meals for guests, and television in the room.

2. That there is a number of aged persons, estimated by the Health Insurance Association of America to be between 3 and 5 million persons 65 years of age and over,[7] who have no desire or need to purchase voluntary health insurance for religious or other reasons. They have methods available for covering hospital charges other than that of purchasing voluntary health insurance. In order to obtain accurate criteria for judging how effectively the voluntary health insurance movement is providing for those who do have a need and a desire for coverage, an adjustment must be made to exclude part of the hospital charges of those aged persons who do not need or want voluntary health insurance aid in paying for hospital bills.

3. That portion of the private total hospital bill arising from those diseases and surgical services normally not covered by voluntary health insurance, such as pulmonary tuberculosis, drug addiction, mental disorders, alcoholism, and cosmetic surgery.

4. That a substantial group of the aged uses the hospital in connection with terminal illness. Recently, the National Office of Vital Statistics of the Public Health Service conducted a study to determine the extent of hospitalization of the recently deceased.[8] This group may comprise a sizable percentage of aged persons who actually used the hospitals. Their methods of paying hospital bills may be different from the methods of those aged who are discharged to their homes or to other institutions. Some of these aged persons may consciously plan to pay for their hospital bills in the last illness by means other than voluntary health insurance. While some may have voluntary health insurance, some of the aged persons who use the hospital in connection with their terminal illness seem to have definite characteristics that suggest separate treatment of part of their hospital bill when dealing with the aggregate hospital costs of persons 65 years of age and over.

5. That portion of the THB due to the chronically ill aged. Most present voluntary health insurance was established to pay part of the bill for those who have acute illness. At the beginning of the 1950's it was not uncommon for Blue Cross Plans to cover payments for only 14 or 21 days of stay in the hospital. Today it is quite unusual to have less than 30 or 60 days hospital stay paid for under the Blue Cross Plans. These plans are still attempting to meet the costs of acute illness. Since this is their purpose, it may be worth while to arbitrarily distinguish between persons going into the hospital for chronic and for acute illness. In the National Health Survey,[9] it was found that 90% of aged persons who went into the short-term general hos-

Table 3.—*Percentage of Health Expenses of Retirees or Persons 65 Years of Age and Over Covered by Voluntary Health Insurance*

	Type of Insurance; % of Charges Paid			
Employer or Insurer	Hospital Expense	Surgical Expense	General Medical Expense	Other
"N" power company (pensioners & dependents 1956.*	84.5	74.8	78.6	...
"B" life insurance company (retired employees) 1957.*	...	...	...	62.0‡
Michigan Hospital Service (data obtained from study of hospital patients, aged 65 and over, with Blue Cross protection).†				
Males	89.0	...	...	...
Females	88.0	...	...	...
"G" corporation (retired employees) 1957.*	94.0	70.0	96.0	...

* Unpublished data.

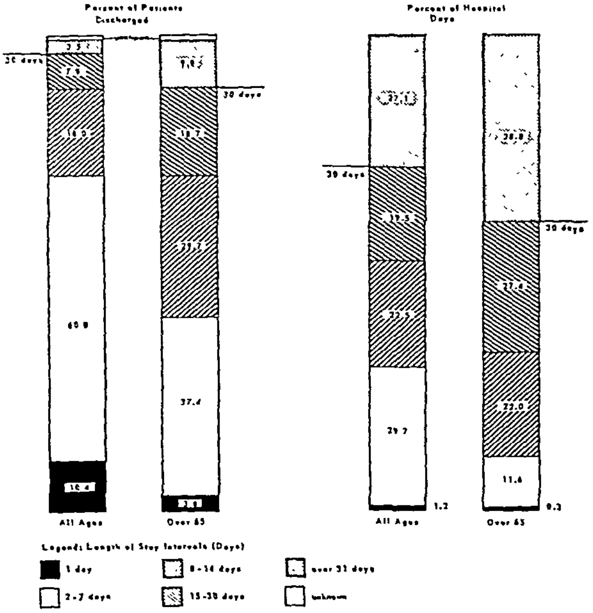
† Lenzer.[5]

‡ % of health care expenses for males in normal retirement.

pital left in 30 days or less (see figure). For these aged patients, voluntary health insurance does have an increasingly important meaning. Some definition of the chronically ill aged person should be adopted. The elimination of this chronic illness hospital cost from the THB should aid us in arriving at a clearer indication of the extent to which voluntary health insurance is meeting the hospital costs of the majority of aged persons.

Comment

A recent survey by the New Jersey Blue Cross Plan has shown that of every 100 claims that have been filed by the entire enrollment, 90 of these claims for hospital stay were paid in full under the comprehensive basic Blue Cross Plan.[10] In addition, 6 of the remaining 10 claims were partially paid by the basic plan; only 4 of the claims went into the extended benefits area. Statistically, only 4 of 100 persons with claims evidently have long or expensive stays in the hospital. But there is an emotional fear among the aged that each will be one of these 4 in 100. Although 90% of persons aged 65 years and over leave the short-term general hospital in less than 30 days, about 38% of patient days in the hospital for aged persons is due to those who remain in excess of 30 days. Even though some of these days may be covered by voluntary health insurance and others may be covered by indigent medical care programs, there is still a fear of the costs of chronic illness among the aged.



Per cent of patients discharged and per cent of hospital days used by length of stay (days), for all ages and those persons aged 65 years and over. National Health Survey, Short-Stay Hospitals, July, 1957, through June, 1958. Source: reference 9.

For a realistic determination of how well the voluntary health insurance movement meets the needs of the majority—that is, over 90% of patients—it is necessary to subtract a portion of the hospital stay of the chronically ill from the statistics. It does little good to say that the aged used two and one-half times as much hospital care as those below age 65. These data should be a comparison of information between those chronically ill at age 65 and those chronically ill below age 65. The problem of the chronically ill is one that is not synonymous with that of the aged. It is a problem that exists among all age groups.

Any type of chronic illness presents a payment problem to the patient. A study of chronic disease carried on by the Commission on Chronic Illness in Baltimore[11] showed the following prevalence of chronic disease as related to the population: Children under 15 years of age had 407 chronic diseases per 1,000 population, or about 4 diseases per 10 children; persons aged 15 to 34 had 1,205 chronic diseases per 1,000; persons aged 35 to 64 had 2,199 chronic diseases per 1,000; and persons 65 years of age and over had 4,042 chronic diseases per 1,000. These raw data must be qualified. While the chronic disease rate presented a consistent picture of increasing with age, the functional consequences of these chronic diseases may be less serious than statistics would indicate. The study of the chronically ill in the Kips Bay section of New York City[12] showed that two of three are able to continue their daily activities, even with their chronic disease. In the year preceding the survey only 1 in 17 required bed care for as long as a month. The Baltimore study[13] showed that the activities of 7 of 10 chronically ill aged persons were not limited.

Hospitalization for chronic illness is not restricted to the aged population. For many of the chronically ill the present voluntary health insurance plans offer an indication of what can be done to aid in meeting hospital expenses. In the Health Information Foundation Survey of 1953,[14] it was found that the annual expenditures for all medical care by those over age 65 was only $102. In a case where continuous medical care is necessary, however, the cost must be met either by the individual or by the family, by the physician and hospital, or by society. A reasonable method of meeting the bills for many of the hospitalized chronically ill may be the use of the Extended Benefit Programs under the Blue Cross–Blue Shield Plans or a "massive major medical" policy by other voluntary health insurance organizations. Under the experimental Massachusetts Blue Cross–Blue Shield Extended Benefits Program it is possible to obtain up to $5,000 voluntary health insurance benefits after retirement.[15]

One firm is already providing a lifetime limit of $15,000 for all medical expenses to its retired employees.[16]

Thinking back that the entire "major medical" field is approximately 10 years old, it may be that $15,000 would be too small for the future. It may be necessary to raise the lifetime limit to $40,000 or $50,000. If a reasonable corridor or deductible is placed on such a policy, in addition to a reasonable coinsurance factor, many persons 65 years of age and over would find it possible to purchase such insurance at the present time, should they choose to do so. Increasing the deductible amount will not eliminate the need for a voluntary health insurance policy to cover the cases of acute illness. A reasonable deductible amount would discourage the use of such a policy for any purpose other than for which it was intended—to handle long-term chronic illness, whether in young or old persons. If this "massive major medical" policy also provides payment for the use of nonhospital facilities and services, such as nursing homes, Visiting Nurses Service, or homemaker service, the cost to the individual person may be lowered. Such policies should soon be developed beyond the experimental stage.

Summary

Present methods of determining the extent of payment by voluntary health insurance mechanisms of the hospital charges of persons 65 years of age and over are inadequate. The data used to develop the current basic formula contain exogenous material which tends to cloud the conclusions; therefore, adjustments must be made to derive accurate statistics. The following points must be considered in making the adjustment: 1. There are some persons who do not wish to purchase an extensive voluntary health insurance program. 2. There is a group of hospital charges that legitimately is not within the purview of voluntary health insurance. 3. There are some persons who neither want nor need voluntary health insurance. 4. Certain diseases and surgical services are not normally covered by voluntary health insurance. 5. There are some persons who use the hospital in connection with their last illness, who have means other than voluntary health insurance intended to cover hospital costs of their terminal illness. 6. Data concerning some of the hospital costs of the chronically ill aged person should be eliminated, since at the present time voluntary health insurance endeavors to cover predominantly acute illness.

These modifications should be made in order to determine the actual information pertinent to a judgment on the extent of voluntary health insurance payment for short-term general hospital care of the aged. At the present time it is not known by what method the exact adjustments can be made. These adjustments can only be the result of careful and continuing research on the hospital utilization by the aged. Without the development of the formulas for adjusting the gross statistics, the present disagreement between survey results and actual voluntary health insurance payments made to the aged to cover short-term general hospital costs will continue.

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MEDICAL NEWS

CALIFORNIA

Fellows Named for Immunology Research.—Dr. William D. McKee, of San Francisco, and Dr. F. Marin Nunez, of Madrid, Spain, are the first participants in the Palo Alto Medical Research Foundation research fellowship program. Both men will work for a year under training grants awarded by the National Institutes of Health, under the direction of Dr. Cutting B. Favour, head of the foundation's department of immunology. The research fellows are chosen and trained primarily for careers in teaching and research.

Personal.—Dr. Adele R. E. Eiler, Los Angeles, has retired from the Bureau of Maternal and Child Health of the Los Angeles County Health Department. A pioneer member of the bureau, which was founded 40 years ago, Dr. Eiler has been its director for the last 13 years.——The 31st annual Arthur Dean Bevan Lecture of the Chicago Surgical Society was given by Dr. William P. Longmire Jr., Los Angeles, professor and chairman, department of surgery, University of California Medical School, on Oct. 2. The title of the lecture was "Gastroesophageal Hemorrhage Associated with Cirrhosis."——Dr. Max Harry Weil, Los Angeles, has relinquished the position of chief of cardiology at the City of Hope Medical Center, Duarte, to join the faculty of the University of Southern California as assistant professor of Medicine. Dr. Bertram J. Allenstein, Los Angeles, has been named acting chief of cardiology at the City of Hope Medical Center, and Dr. Weil will continue as a consultant in the department of cardiology at that institution.

COLORADO

New Hospital in Colorado Springs.—The new Penrose Hospital in Colorado Springs, which began as a 25-bed sanitarium, was dedicated Sept. 15. The new 12-story, 311-bed structure was built at a cost of $7,500,000. Ground breaking was on Nov. 3, 1956, followed by a campaign in which the two largest contributions were made by the El Pomar Foundation and the late Mrs. Julie Penrose (a total of $3,200,000), and by the Donner Foundation in memory of William H. Donner (totaling $237,100). Mrs. Penrose was the wife of Spencer Penrose, who had created the El Pomar Foundation to carry on philanthropic works. After the death of Mr. Penrose in 1939, Mrs. Penrose continued the foundation works, including a $250,000 contribution toward the Penrose Cancer Clinic. The new hospital contains the Dr. Gerald Bertram Webb Library, a memorial to the physician who served more than half a century on the staff of the Glockner-Penrose Hospital. The pediatrics section on the fourth floor includes indoor and outdoor play areas. Other facilities include a central pharmacy, physical and occupational therapy departments, the Glockner tuberculosis treatment floor (fifth), and a floor for future use by self-care patients (twelfth). The hospital, run by the Sisters of Charity, has a staff of 450. Sister Cyril is the hospital administrator.

CONNECTICUT

Dr. Gordon Wins Gastroenterology Award.—The American College of Gastroenterology announced that the 1959 Henry G. Rudner Sr. Award "for the best unpublished paper on gastroenterology or an allied subject" was given to Dr. Martin E. Gordon, of New Haven. Dr. Gordon, assistant clinical professor of medicine at Yale University School of Medicine, presented his paper, "The Acute Effects of Abdominal Paracentesis in Laennec's Cirrhosis upon Exchanges of Electrolytes and Water, Renal Function and Hemodynamics," at the 24th annual meeting of the college. The award consists of a cash prize of $750.

ILLINOIS

Chicago

Full-Time Pathologist for Coroner's Office.—Dr. Joseph E. Campbell, formerly forensic pathologist and director of laboratories for Philadelphia, was recently appointed Cook County's first full-time pathologist with the coroner's office. Certified in pathological anatomy by the American Board of Pathology, Dr. Campbell received his M.D. from Harvard Medical School, Boston, and later served on the staff of Ohio State University, Columbus, before going to Philadelphia. A civic committee including Dr. Lowell T. Coggeshall, dean of the biological sciences, University of Chicago, helped in the selection of Dr. Campbell.

Dustfall in Chicago.—A report of the chemical analysis of dustfall for Chicago by the Armour Research Foundation of the Illinois Institute of Technology reveals that the highest total dustfall for

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

July was observed in the Loop area, with a single Loop station reporting a high of 185.5 tons per square mile per month of 30 days. The Loop average was 156.9 tons. This consisted of 28.2 tons of water insoluble constituents and 128.7 tons of water soluble constituents. The lowest reading for the month was reported from a north side station. The adjusted average total dustfall for the city (excluding the Loop) was 47.0 tons per square mile per month of 30 days.

Break Ground for Research Institute.—Groundbreaking ceremonies for the Chicago Medical School's new Medical Research Institute were held Sept. 18. The 10-story, block long, 110,000 square foot building is the first of several buildings to be erected on the school's 10-acre campus in the West Side Medical Center, bounded by Harrison, Damen, Ogden, Polk, Dekalb, and Hoyne streets. The land was acquired for the school through a gift from the Max and Leola Epstein Foundation. The U. S. Public Health Service awarded the school one million dollars for the building and $121,696 for moveable equipment within the building itself. The total cost of the building will be about 4 million dollars. Completion is scheduled for the fall of 1960. The new institute will provide research facilities for over 400 scientists, technicians, and postgraduate students. On each side of the main lobby, there will be exhibit halls, one of which will be devoted to basic research and the other to applied or clinical research. The building will be provided with closed circuit TV. There will also be a large photography department and a section for ceramics and the building of special exhibits. Offices and laboratories are on the perimeter of the air-conditioned building. The animal quarters will have a special climate control.

KENTUCKY

State Medical Election.—The Kentucky State Medical Association, at its recent annual meeting installed Dr. Irvin Abell Jr., Louisville, as president and elected Dr. Richard G. Elliott, II, Lexington, as president-elect, to take office at the 1960 annual meeting. Other officers elected were: vice-presidents, Dr. David M. Cox, Louisville, (central), Dr. William O. Preston, Lexington (eastern), and Dr. Rex E. Hayes, Glasgow (western). Dr. Woodford B. Troutman, Louisville, was reelected secretary, and Dr. Delmas M. Clardy, Hopkinsville, was reelected treasurer. Speaker for the House of Delegates is Dr. Sam A. Overstreet, Louisville.

MASSACHUSETTS

Dr. Keefer Named Director of Medical Center.—Dr. Chester S. Keefer, of Boston, director and dean of the Boston University School of Medicine since 1955 and president-elect of the American College of Physicians, was appointed director of the newly created Boston University–Massachusetts Memorial Hospitals Medical Center. Dr. James M. Faulkner, of Cambridge, is chairman of the joint administrative board of the Center. Dr. Keefer has resigned as dean and chairman of the department of medicine at the School of Medicine to accept this new position. Dr. Lamar Soutter, associate dean and professor of surgery, was appointed acting dean of the school. Dr. Keefer, Wade professor of medicine at the School of Medicine, has taught at Johns Hopkins University and Hospital, the University of Chicago, Peiping Union Medical College in China, and served on the Harvard Medical School faculty for 10 years.

MICHIGAN

Dr. Graham Goes to Canada.—Dr. Bruce D. Graham, professor of pediatrics at the University of Michigan Medical Center, Ann Arbor, was appointed chairman of the department of pediatrics at the University of British Columbia in Vancouver, Canada. He will assume his new position in November. Dr. Graham joined the Medical Center staff after receiving his M.D. degree from Vanderbilt University, Nashville, Tenn., in 1942. He is a diplomate of the American Academy of Pediatrics.

Faculty Health Examinations.—The 1,000th faculty member of the University of Michigan, Ann Arbor, began his two-week executive-type health examination Sept. 9 under a program launched three years ago. Elective, confidential, and free of charge, the examinations were established to maintain the health of the faculty and to check any disorders before they reach serious proportions. Invitations for the health appraisal originally went to faculty members above age 60. Gradually, the age level has been reduced so that present invitees are in the 30 to 40 age bracket. Dr. Charles J. Tupper, associate professor of internal medicine, is director of the faculty health project. He reported that 75% of those invited to have the examination have accepted.

MINNESOTA

Symposium on Automobile Trauma.—All physicians are invited by the new Methodist Hospital of St. Louis Park (Minneapolis) to attend an all-day symposium at the hospital Nov. 14 on the subject, "Automobile Trauma." Guest speakers include Dr. Fiorindo A. Simeone, professor of surgery, Western Reserve University, Cleveland; and Dr. Dana M. Street, chairman, department of orthopedics, University of Arkansas, Little Rock. Physicians and their wives are invited to attend the dinner at the Radisson Hotel at Minneapolis following this symposium. In the evening, "Safety on the Highway" will be discussed. Included in the evening program is the Hon. Kenneth A. Roberts, of the House of Representatives. Seven hours of category I credit will be given by the American Academy of General

Practice for attendance. Information may be obtained from Dr. Reuben Berman, Program Chairman, Methodist Hospital, St. Louis Park 26, Minn.

MISSOURI

Dedicate Rehabilitation Institute.—Formal dedication of the Irene Walter Johnson Institute of Rehabilitation at the Washington University–Barnes Hospital Medical Center will be held at 8 p.m., Thursday, Oct. 29, in the auditorium of the Medical School, Dean Edward W. Dempsey announced. A tour of the $800,000 institute, located at 509 S. Euclid Ave., will follow the formal ceremony. First patients were admitted to the new building Oct. 1. There are accommodations for up to 100 patients per day. Activities of the institute will be coordinated through the department of preventive medicine and public health. Dr. Eric Reiss, assistant professor of medicine and of preventive medicine, is institute director. The institute is the first of three new buildings to be completed at the Medical Center. The concrete frame has been poured for 5 of the 10 floors of the $2,252,785 Spencer T. Olin Residence Hall for medical students, for which ground was broken last November. The dormitory is expected to be ready for occupancy by September, 1960. Contractors are now raising the concrete frame for the David P. Wohl Jr. Memorial –Washington University Clinics, with construction planned for completion in January, 1961. The 12-story $3,415,886 structure was begun last November.

MONTANA

State Medical Election.—At a meeting of the House of Delegates of the Montana Medical Association in Butte Sept. 19, the following officers were elected for the term ending at the close of the 1960 annual meeting: Dr. Leonard W. Brewer, Missoula, president; Dr. Raymond F. Peterson, Butte, president-elect; Dr. Everett H. Lindstrom, Helena, vice-president; Dr. William E. Harris, Livingston, secretary-treasurer; and Dr. Jesse T. Schwidde, Billings, assistant secretary-treasurer.

NEW YORK

Dedicate Biological Laboratory.—Dedication ceremonies at the new $954,000 Biological Laboratory of Roswell Park Memorial Institute were held Sept. 25 at Springville, N. Y. Roswell Park Memorial Institute is the state's cancer research facility. The Biological Station at Springville, located about 35 miles from Roswell Park in Buffalo, was organized as a part of the institute in 1913. Presiding at the dedication program was Dr. George E. Moore, Buffalo, director of Roswell Park. Dr. Herman E. Hilleboe, state health commissioner, was the principal speaker. The new biological laboratory is equipped for services in radiobiology, physiological genetics applied to the studies on normal and malignant pigment formation, embryology, and tissue culture and biochemistry. The basement of the new building will be used for studies in radiobiology. One laboratory is equipped with a 250,000 volt x-ray machine for short-term experiments on small mammals, while two others will be used for long-term studies on effects of radiation on various species of animals.

Report on Pollen Sampling.—Daily pollen counts from the state's pollen sampling network indicate ragweed is creating a serious problem for many residents of New York State, Dr. Herman E. Hilleboe, state health commissioner and chairman of the New York State Air Pollution Control Board, reported. The pollen sampling network, sponsored by the Air Pollution Control Board, consists of 16 stations. Thirteen of the stations make daily pollen counts available to residents of the State through newspapers, radio, and television stations. Three other stations do not make daily reports, but figures from these will be published in an annual ragweed pollen index. Highest sampling station pollen count during August was 1,288, reported in Cobleskill, Aug. 31. Highs reported from other stations were: Melrose, 988, Aug. 31; Troy, 474, Aug. 27; Warsaw, 318, Aug. 31; Batavia, 236, Aug. 26; Poughkeepsie, 228, Aug. 27; Albany, 166, Aug. 27 and 31; Hudson, 158, Aug. 29; Ithaca, 110, Aug. 27; Hornell, 96, Aug. 30; Yonkers, 67, Aug. 31; Tupper Lake, 62, Aug. 24; and Corning, 49, Aug. 26. Counts between 5 and 25 indicate the atmosphere has been moderately contaminated with pollen. Pollen counts above 25 are capable of producing hay fever symptoms.

New York City

Merge Neurosurgery and Surgery Departments.—The department of neurosurgery at the State University of New York Downstate Medical Center was merged with the department of surgery. Following the retirement Sept. 1 of Dr. E. Jefferson Browder, who has headed a separate department of neurosurgery since 1952, the move returned neurosurgery to its former status as a division of the department of surgery. Headed by Dr. Clarence Dennis, chairman, the department of surgery will now include five separate divisions in addition to general surgery: neurosurgery, ophthalmology, orthopedic surgery, otorhinolaryngology, and urology. Because the Kings County Hospital services correspond to the teaching departments of the Medical Center and are headed by the chairmen of these departments, neurosurgery will become a division of surgery in the hospital also. The division of neurosurgery at both the Medical Center and the hospital will be headed by Dr. Albert W. Cook, assistant professor of neurosurgery.

University News.—Dr. E. Jefferson Browder, chairman, department of neurosurgery State University of New York Downstate Medical Center, retired from active service on the faculty and has been named professor emeritus of neurosurgery effective Sept. 1. Dr. Browder has been on the faculty for 34 years. He has been chairman of the department of neurosurgery since 1952, prior to which he served as chairman of the department of surgery. —Dr. Brian MacMahon, head, department of epidemiology at Harvard University School of Public Health, Boston, was named professorial lecturer at the State University of New York Downstate Medical Center. Formerly a full-time associate professor of environmental medicine and community health at the Downstate Medical Center, Dr. MacMahon will return during the year to deliver several lectures on epidemiological problems. Dr. MacMahon, a native of Sheffield, England, received his medical education at the University of Birmingham and taught there for six years before moving to the United States in 1955.

NORTH CAROLINA

Organize Postoperative Nursing Team.—A new postoperative nursing team was organized at the Duke University Medical Center to provide special intensive care for surgical patients. The team consists of seven graduate nurses who are undergoing a six-week training period in specialized postoperative nursing care. Facilities and equipment for this care will be located in Duke Hospital's intensive nursing unit. Emphasis will be on the care of patients who have had open heart operations to repair congenital defects inside the heart.

OHIO

Dedicate Research Building.—The University of Cincinnati College of Medicine's new William B. Wherry Medical Research Building was formally opened Sept. 21 in ceremonies in the main College of Medicine building. Dr. Charles A. Doan, Columbus, dean of the Ohio State University College of Medicine, was the principal speaker. The new four-story brick building houses research and graduate training facilities for the basic sciences of biological chemistry, microbiology, physiology, pharmacology, and preventive medicine. The $1,750,000 structure adjoins the main medical college building. Presiding at dedication ceremonies were UC's Dr. Walter G. Langeam, president, and Dr. Stanley E. Dorst, medical dean. Mayor Donald Clancy represented the city of Cincinnati. Dr. Gustav Eckstein, professor of physiology, paid tribute to his friend, the late Dr. Wherry, for whom the building was named. Dr. Wherry, a bacteriologist who discovered tularemia in humans, was for many years head of UC's department of bacteriology and hygiene. Built with funds voted by the city and a $875,688 matching federal grant, the new Wherry Hall is headquartes for much of the university's more than 2 million dollars yearly medical research.

PENNSYLVANIA

Open Research Building at Bushy Run.—Pittsburgh's 46-year-old Mellon Institute, officially opened the Bushy Run Laboratories, 25 miles east of the city's Golden Triangle, on Sept. 22. The Bushy Run research facilities consist of the Chemical Hygiene Building and the Radiation Research Building, the first two in a series of proposed special buildings, each devoted to a particular field of investigation. The project represents an expansion of Mellon's activities and supplements the facilities of the institute's main building in Pittsburgh. Gen. Matthew B. Ridgway is chairman of the Board of Trustees of Mellon Institute. The laboratory structures at Bushy Run face a grass-covered mall at the high point of a 230-acre tract of Westmoreland County countryside.

Deaths from Cancer.—Cancer held its place as the second leading cause of deaths in Pennsylvania last year (1958) accounting for 18,856 fatalities, it was announced by the State Health Department's Division of Statistics and Records. Outranked as a cause of death only by heart disease, cancer accounted for about one out of every six deaths in the state during the year. The statistics indicated the digestive system as the primary site of the malignancy in 37% of the deaths; the genitourinary system in 19%; the respiratory system in 14%; and the breast in 9%. Leukemia and Hodgkin's disease constituted 6% of the total cancer deaths; cancer of the buccal cavity and pharynx, 2%. Cancer of other sites—skin, eyes, bone, endocrine glands, nervous system, and connective tissue—comprised the remaining 12% of the total deaths from the disease. The Pennsylvania rate from cancer in 1958, according to the statistics, was 169.9 per 100,000 population, a slight decrease from the previous year's record rate of 170.8 but 11% higher than the 1950 rate of 155.3.

Philadelphia

Dr. Koprowski Honored.—Dr. Hilary Koprowski, director of the Wistar Institute, was made an officer of the Belgian Royal Order of the Lion Sept. 21 "in recognition of a polio immunization program which he has initiated in the Belgian Congo for the Wistar Institute." Mr. Rene Merenne, cultural attache of the Belgian Embassy in Washington, represented the King of the Belgians in conferring the decoration on Dr. Koprowski. The Belgian Congo immunization project aims to protect the population of 12,660,000 against poliomyelitis with Wistar Institute oral live vaccine originated by Dr. Koprowski. About 400,000 persons in the Congo have received the vaccine thus far.

Personal.—Dr. Robert L. Lambert was named medical director of the Hospital of the Woman's Medical College, effective Sept. 1, succeeding Dr. Eva Fernandez Fox, who continues her association with the college as a member of the department of radiology and medicine.—Dr. William H. Schmidt was feted at a testimonial dinner June 24. Dr. Schmidt recently relinquished his duties as head of the department of physical medicine at Jefferson Medical College and Hospital to become emeritus professor. Toastmaster for his memorial occasion was Dr. George Morris Piersol. Dr. Herman L. Rudolph, of Reading, delivered the curriculum vitae address and a silver plaque commemorating the occasion was presented by Dr. William A. Sodeman, dean of Jefferson Medical College.

Fund to Aid Students.—A $150,000 fund "to aid worthy students of Medical School" was established at the University of Pennsylvania in memory of Cornelia Warren Hopeman, of Waynesboro, Va., and in honor of Dr. Truman G. Schnabel, emeritus professor of medicine. The Truman G. Schnabel Fund, as it is called, was created through the wills of two of Dr. Schnabel's former patients—Mrs. Hopeman and her husband, Bertram C. Hopeman, an industrialist. They had come under the internist's medical care when they lived at Moylan, Pa. Mrs. Hopeman died in 1951 and Mr. Hopeman died in 1958. The principal of the fund will be invested by the university and the income made available to medical students needing financial aid. Dr. Schnabel, in private practice in Philadelphia, was graduated from the School of Medicine in 1911 and served on its faculty from 1914 until his election as emeritus professor in 1951.

WASHINGTON

Annual Strauss Lecture.—On Friday, Nov. 6, Dr. J. Garrott Allen will give the 10th annual Alfred A. Strauss Lecture sponsored by the department of surgery of the University of Washington School of Medicine, Seattle. Dr. Allen, head of the department of surgery at Stanford University School of Medicine, San Francisco, will present "Serum Hepatitis." The lecture will be held in the Auditorium of the Health Sciences Building of the university at 8:15 p. m. Previous Strauss Lecturers have included Dr. Alfred A. Strauss, Chicago; Dr. Dallas B. Phemister, Chicago; Dr. Warren H. Cole, Chicago; Dr. Owen H. Wangensteen, Minneapolis; Dr. Lester R. Dragstedt, Chicago; Dr. Frederick C. Coller, Springfield, Mo.; Dr. Edward D. Churchill, Boston; and Dr. Alfred Blalock, Baltimore.

Dedicate School Building for the Blind.—Dedication of the Irwin Educational Building, combination school, library, and auditorium, at the School for the Blind, Vancouver, has been set for Nov. 7. Governor Albert D. Rosellini will be present for the ceremonies. The structure was used for the first time with the opening of school Sept. 8. Registration totaled 122 students. The rectangular building encloses a patio and encompasses some 36,000 square feet. It cost $520,500. It contains 17 classrooms; a music wing housing a music library, two studios, a recording studio and 12 sound-proof private practice rooms; a home economics section; a large centralized library; and an auditorium with capacity seating at 300. The building contains no steps, with the exception of those to the auditorium stage. The building will take care of educational needs from preschool through high school. The school has a staff of 20 teachers, four of whom are blind. The institution has three residential units, which accommodate 15 students each. More than 80% of the children make their residence on the campus during the school year. The late Robert Irwin, first graduate of the School for the Blind, for whom the Educational Building is named, was the first blind man to receive France's highest honor, the Chevalier of the Legion of Honor. Western Reserve University bestowed on him its honorary doctor of laws degree.

GENERAL

Congress of Surgeons in Honolulu.—The eighth congress of the Pan-Pacific Surgical Association will be held in Honolulu, Hawaii, Sept. 28-Oct. 5, 1960. All members of the medical profession are cordially invited. The scientific program will include nine surgical specialty sections to be held simultaneously. Information and brochures may be obtained by writing Dr. Forrest J. Pinkerton, Director General, Pan-Pacific Surgical Association, Suite 230, Alexander Young Building, Honolulu 13, Hawaii.

Essay Contest on Chest Diseases.—The American College of Chest Physicians is offering three cash awards to winners of the 1960 prize essay contest. First prize will be $500, second prize $300, and third, $200. Each winner will receive a certificate. The contest is open to undergraduate medical students throughout the world. Essays may be written on any phase of the diagnosis and treatment of chest diseases (cardiovascular or pulmonary). The contest closes April 1, 1960. For application and information, write the American College of Chest Physicians, 112 E. Chestnut St., Chicago 11.

Meeting of Neurological Surgeons.—The annual meeting of the Congress of Neurological Surgeons will be held at the Americana Hotel, Miami, Fla., Oct. 28-31. The honored guest will be Dr. William J. German, New Haven, Conn. The meeting is oriented toward various aspects of the brain tumor problem. On Wednesday morning, Oct. 28, a half-day postgraduate course on neuropathology will be conducted by Dr. Louise C. Eisenhardt, New Haven, Conn. For information, write Dr. Richard L. DeSaussure Jr., Secretary-Treasurer, Suite 101 B, 20 S. Dudley St., Memphis, Tenn.

Forum on Medical Economics.—The Medical Economics Forum was established in Oradell, N. J., to conduct a continuing program of practice management conferences for physicians. The forum will operate as a division of Medical Economics, Inc., publishers of *Medical Economics.* Forum meetings are to be held in large cities from coast to coast. The meetings will bring to physicians authorities in patient handling, law, accounting, taxes, insurance, investments, estate planning, and hospital and professional relations. The Medical Economics Forum has been set up as a complete and separate enterprise with its own staff. The executive director is Mr. Richard Cliggott.

Southwest Meeting on Obstetrics and Gynecology.—The ninth annual meeting of the Southwest Obstetrical and Gynecological Society will be held Nov. 2-3 in Palm Springs, Calif., with headquarters in the Mirador Hotel, under the presidency of Dr. Charles J. Newcomb, Tucson, Ariz. The program includes the following speakers: Drs. Ralph C. Benson, Portland, Ore.; Russell R. de Alvarez, Seattle; Bernard J. Hanley, Los Angeles; Charles E. McLennan, San Francisco; Daniel G. Morton, Los Angeles; Ernest W. Page, San Francisco; and Ralph R. Reis, Chicago. A symposium on cancer is planned for the morning of Nov. 3, with Dr. Jesse A. Rust Jr., San Diego, Calif., presiding. Dr. Reis will moderate a round-table discussion following the symposium. The banquet will be held Nov. 3, 7:30 p. m.

Society for Tropical Dermatology Formed.—During the sixth International Congress for Tropical Medicine in Lisbon in September, 1958, the formation of an International Society for Tropical Dermatology was proposed. An organizing committee composed of Prof. Dr. Aldo Castellani, Instituto de Medicina Tropical, Lisbon; Dr. Anthony Cipollaro, New York City; and Dr. Frederick S. Reiss, New York City, general organizing secretary, has been formed. Dermatologists, pathologists, and microbiologists of the United States, Canada, Central and South America, Europe, Africa, Asia, and Australia have joined and the charter membership has reached about 800. It has been tentatively agreed that the first meeting will be held in 1963 in Rio de Janiero in conjunction with the congress of the International Association for Leprosy.

Heart Disease in Children.—Heart disease is responsible for about 10,000 deaths a year in the United States among children under 15 years of age, it is reported by statisticians of the Metropolitan Life Insurance Company. Congenital malformations of the heart account for a large majority of these deaths. Rheumatic fever and chronic rheumatic heart disease cause about 300 of the deaths, and all other diseases of the heart add over 800 deaths to the total. Childhood mortality from the heart disease is heavily concentrated in infancy. Among white boys in the United States in 1955-1957, the death rate dropped sharply from 235 per 100,000 under age 1 year to 7 at ages 1-4, and further to 3 at ages 5-9. The marked reduction in heart disease mortality after infancy reportedly reflects the failure of children with severe forms of congenital heart disease to survive beyond the first year. The small rise at ages 10-14 represents primarily the increase in the death rate from rheumatic heart diseases.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	Sept 26, 1959 Paralytic Type	Sept 26, 1959 Total Cases	Sept. 27 1958 Total
New England States			
Maine	15	15	..
New Hampshire	1	1	..
Vermont	..	..	1
Massachusetts	8	10	..
Rhode Island	1	2	..
Connecticut	4	4	..
Middle Atlantic States			
New York	17	32	19
New Jersey	14	17	22
Pennsylvania	16	18	10
East North Central States			
Ohio	7	19	22
Indiana	1	10	6
Illinois	7	20	23
Michigan	10	29	159
Wisconsin	1	2	5
West North Central States			
Minnesota	16	18	..
Iowa	7	31	2
Missouri	15	32	10
North Dakota	..	1	2
South Dakota	..	1	1
Nebraska	2	5	2
Kansas	4	10	3
South Atlantic States			
Delaware	..	..	1
Maryland	4	5	1
District of Columbia	..	..	..
Virginia	23	26	14
West Virginia	9	10	15
North Carolina	9	13	4
South Carolina	1	5	1
Georgia	4	6	..
Florida	3	5	4
East South Central States			
Kentucky	10	14	..
Tennessee	9	14	7
Alabama	11	12	2
Mississippi	3	6	5
West South Central States			
Arkansas	10	20	2
Louisiana	3	3	5
Oklahoma	5	7	1
Texas	16	28	20
Mountain States			
Montana	..	..	1
Idaho	..	..	2
Wyoming	..	..	..
Colorado	..	1	2
New Mexico	2	3	..
Arizona	4	5	..
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	9	9	..
Oregon	5	6	4
California	17	20	8
Alaska	1	1	..
Hawaii	1	1	1
Territories and Possessions			
Puerto Rico	..	..	..
Total	305	497	387

Society Honors Two Physicians.—Dr. Lester R. Dragstedt, Chicago, received the 1959 Honor Award given by the Mississippi Valley Medical Society Sept. 30. Dr. Dragstedt, a pioneer in research in gastric physiology, is a professor emeritus at the University of Chicago and professor of surgery at the University of Florida School of Medicine, Gainesville. The Honor Award is given from time to time to nonmembers of the society "who have made distinguished contributions to clinical medicine." Dr. Joseph C. Edwards, St. Louis, received the 1959 Distinguished Service Award given by the Mississippi Valley society, of which he is the immediate past-president. The award was presented to Dr. Edwards Sept. 30. The Distinguished Service Award is given annually to a fellow of the society "who has rendered unusual and distinguished service to the medical profession."

Southwestern Medical Meeting.—The 44th annual meeting of the Southwestern Medical Association will be held Nov. 5-7, at Roswell, N. M., in association with the New Mexico Chapter, American Academy of General Practice, and the Chaves County Medical Society. The program includes the following speakers: Dr. Frederick R. Guilford, Houston, Texas; Dr. Jack S. Guyton, Detroit; Dr. James W. Headstream, Little Rock, Ark.; Dr. Paul C. Laybourne Jr., Kansas City; Dr. Dan G. McNamara, Houston; Dr. James S. Miles, Denver; Dr. Edward B. D. Neuhauser, Boston; Dr. Edith L. Potter, Chicago; Dr. Willis J. Potts, Chicago; and Dr. Frederic A. Speer, Kansas City. Question-and-answer sessions will be held on each afternoon. The program is approved for 12 hours of category I credit by the American Academy of General Practice. An interim session of the House of Delegates of the New Mexico Medical Society will be held Nov. 5.

Annual Meeting on Medical Colleges.—The 70th annual meeting of the Association of American Medical Colleges, will be held Nov. 2-4 at the Edgewater Beach Hotel, Chicago. Dr. John M. Mitchell, dean, University of Pennsylvania, Philadelphia, will present "Medical Schools Are the Keystone of Medical Progress" as the presidential address the morning of Nov. 2, followed by "Medical Education and Public Health Service," presented by Dr. Leroy Burney, surgeon general, United States Public Health Service. The 1959 teaching institute, the second institute of clinical teaching, will be held the afternoon of Nov. 2, with Dr. Charles G. Child, III, Ann Arbor, Mich., as chairman. Simultaneous sessions are planned for the morning and afternooon of Nov. 3. A business meeting will be held the morning of Nov. 4. A program of activities for wives is planned. For information, write Dr. Ward Darley, Executive Director, 2530 Ridge Ave., Evanston, Ill.

Course in Applied Epidemiology.—A course in applied epidemiology will be offered by the Communicable Disease Center, Public Health Service, at Denver, Nov. 16-20 as a part of the continuing program of the center's training branch. This course is designed primarily for physicians who serve as investigators of disease outbreaks or have administrative responsibility for such investigations. It serves as a refresher and an introductory course. Emphasis is placed on developing and understanding use of epidemiological techniques. Lecture-discussion sessions and audiovisual aids are used. Group participation is obtained through the utilization of the group solution of epidemiological problems, seminar-type presentations, and panel discussions. Registrants will be expected to attend all sessions. Information and application forms may be obtained from: Chief, Communicable Disease Center, Public Health Service, 50 Seventh St., N. E., Atlanta 23, Ga., Attention: Chief, Training Branch; or from Public Health Service, Region VIII, First National Bank Building, Denver 2.

Surgeons Name Honorary Fellows.—Dr. Louis M. Orr, Orlando, Fla., President, American Medical Association was one of 12 persons named to receive honorary fellowships from the International College of Surgeons in September. The others included Mother Anna Marie Dengel, superior general of the Medical Mission Sisters, Rome, Italy, a physician and founder of a medical service to people in underdeveloped countries; Dr. Jean Creyseel, University of Lyon, France; Dr. Sten A. Friberg, Karolinska Institute, Stockholm, Sweden; Rear Adm. Bartholomew W. Hogan, MC, USN, surgeon general and chief of the Bureau of Medicine and Surgery, United States Navy, Washington, D. C.; Dr. Arnold S. Jackson, chief of staff of the Methodist Hospital, Madison, Wis.; Dr. Donatien Marion, governor of the University of Montreal, Canada; Dr. Samuel Rosen, Columbia University College of Physicians and Surgeons, New York; Dr. Cutice Rosser, University of Texas Southwestern Medical School, Dallas; Dr. Ralph E. Snyder, New York Medical College, New York; Dr. J. Andre Thomas, Faculty of Sciences, the Sorbonne, Paris; and Dr. Pietro Valdoni, University of Rome, Italy. Mother Dengal, the first woman to receive an honorary fellowship from the college, established 30 hospitals in India, Pakistan, Indonesia, Africa, and Venezuela.

FOREIGN

Exhibition of Medical Photography.—The Medical Group of the Royal Photographic Society will present an exhibition of Medical Photography at the society's house, 16 Princes Gate, London, S. W. 7., Nov. 12-19. The formal opening of the exhibition will be made by Dr. H. Clegg, editor of the *British Medical Journal*, on Thursday, Nov. 12, at 6:30 p. m. Following the distribution of awards, and a period for viewing the exhibits, Dennis Segaller, B.Sc., of the Shell Film Unit, will lecture on film animation.

Congress on Occupational Medicine.—A Congress on Occupational Safeguards and Occupational Medicine will be held in Dusseldorf, Germany, Nov. 12-14. The congress will be under the patronage of the Federal Minister of Labor and Social Organization, Theodor Blank. The general section will convene Thursday, Nov. 12. The main subject to be presented by Prof. O. Fitz, of Vienna, will be "Exhaustion, the Disease of Our Time and Its Prevention by Organically Correct Work Performance." A round-table discussion will be concerned with "Modern Safeguards and Protective Devices." A lecture, "Protection Against Ionizing Rays in Industrial Plants," will be presented by O. Vaupel, Dr. Phil. A round-table discussion will consider "Improvement of Occupational Safeguards in Industry." In the medical section, with Dr. K. H. Lowen, as chairman, Dr. H. Schneider, will present "Pulmonary Emphysema and Bronchitis as Occupational Diseases," and Dr. P. E. Rosenberger, will give "Occupational Exposure to Heat and Respiratory Insufficiency." Other subjects to be presented will be "The Human Factor in Industrial Enterprises" and "Occupational Wear and Tear in the Human Motor Apparatus."

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8. Final date for filing application is January 8. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* For candidates on the East Coast, Nov. 6-7, 9-10. Final date for filing application was March 1. *Oral.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application was Aug. 15. *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications is Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application was October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Washington, Dec. 4-6. *Written.* Jan. 8. Final date for filing application for the written examination is Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application was July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Closing date for filing applications was August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Oral examinations (Part II):* Cincinnati, Nov. 9-10; Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

GOVERNMENT SERVICES

AIR FORCE

Personal.—Brig. Gen. John K. Cullen became deputy surgeon of the U. S. A. F. in August, succeeding Major Gen. Olin F. McIlnay.

ARMY

Meeting of Military Surgeons.—Reserve retirement point credits may be earned by medical service reserve officers who attend the daily sessions of the 66th annual convention of the Association of Military Surgeons to be held at the Mayflower Hotel, Washington, D. C., on Nov. 9-11, 1959. Those who can earn points include eligible physicians, dentists, nurses, veterinarians, Army medical specialists, and Medical Service Corps officers of the Army, Navy, and Air Force Reserves. The awarding of credits will be based on one point for each day of attendance at the meeting, if the session attended is two hours or more in length. Not more than one point may be earned per day. The convention theme will be "The Practice of Military Medicine—Broadening Concepts."

After the opening remarks by Major Gen. Harold H. Twitchell, U. S. A. F., M.C., president of the association, there will be a panel of chiefs of federal medical services. Appearing on the panel will be Dr. Frank Berry, assistant secretary of defense (health and medical); Lieut. Gen. Leonard D. Heaton, Army surgeon general; Rear Adm. Bartholomew W. Hogan, Navy surgeon general; Major Gen. Oliver K. Niess, Air Force surgeon general; Dr. Leroy E. Burney, Public Health Service surgeon general; and Dr. William S. Middleton, chief medical director of the Veterans Administration.

Personal.—A promotion to brigadier general, reserve, recently went to Col. James H. Kidder, who has served as special assistant for reserve affairs to the Army surgeon general since July, 1955.

NAVY

New Toxicology Unit.—Quarters for the new toxicology unit were completed in October. The unit contains quarantine spaces; an animal food preparation kitchen; cage washing facilities; pathology, chemistry, and physics laboratories; and animal inhalation exposure cubicles. The purpose of the unit will be to provide technical and specialized services in the fields of operational toxicology and health engineering as related to toxicity problems encountered aboard ships. It will also develop and provide biological data necessary for determining permissible limits so that precautionary measures, conducive to good health practices, may be prescribed.

Personal.—Capt. Lloyd B. Shone was appointed director of the preventive medicine division in the bureau of medicine and surgery. The division is responsible, under the surgeon general of the Navy, for establishing and promulgating preventive medicine practices throughout the naval establishment on a global basis.

NATIONAL ACADEMY OF SCIENCES

New Fellowship in Radiology.—On behalf of the James Picker Foundation, the National Academy of Sciences–National Research Council announces a new fellowship program, designed in the interests of academic radiology. These advanced fellowships are offered in addition to the previously established research fellowships and scholar and research grants, which will be continued during 1960-1961. The new awards are planned to prepare the candidate to meet in full the intellectual demands of an academic position in radiology. Emphasis is placed on the acquisition of a broad background in the basic sciences related to radiology.

In general, it is expected that the candidate will be not more than 33 years of age and will have completed his clinical training. He should be prepared to devote a minimum of two years to course work in the basic sciences, to the application of the techniques and methods of these basic disciplines to radiologic research, and to other activities designed to enhance his preparation for an academic career. The details of his program will be worked out on an individual basis through consultation between the candidate, his clinical and academic advisers, and the members of the Academy–Research Council's committee on radiology. Applications will be accepted on nomination by a clinical adviser, who should be a member of the staff of a department of radiology in a medical school.

The previously established program of the foundation, for which applications again are being invited, comprises three types of awards. 1. Postdoctoral fellowships in radiology research are open to recent graduates who desire experience and training in scientific investigation. While persons from closely related disciplines are eligible to apply, candidates with some training in the field of radiology will receive preference under this program. Applicants must hold the M.D., Ph.D., or Sc.D. degree or the equivalent. Awards are for a period of one year, but requests for renewal will be considered. 2. Grants for scholars are a transitional form of support, designed to bridge the gap between the completion of research fellowship training and the period when the young scientist has thoroughly demonstrated his competence as an independent investigator. The application is submitted by the institution on behalf of the prospective scholar. If the request is approved, a grant of $6,000 per year is made directly to the institution as a contribution toward the scholar's support, or his research, or both. Initial grants are limited to one year, but renewal for two additional years may be recommended. 3. Grants-in-aid of research are designed to encourage investigations offering promise of improvement in radiologic methods of diagnosis or treatment of disease. Research grants are awarded to institutions rather than to persons. In line with the interests of the foundation, the program is oriented toward, but not necessarily limited to, the diagnostic aspects of radiology.

Applications in these categories will be reviewed by the committee on radiology of the Academy–Research Council's division of medical sciences. Final determination of awards is made by the foundation on recommendation of the division. Support is not restricted to citizens of the United States or to laboratories within this country.

Applications for the fiscal year 1960-1961 should be submitted by Dec. 15, 1959. Further details and application blanks may be obtained from the Division of Medical Sciences, room 411, National Academy of Sciences—National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C. The National Research Council of Canada serves as scientific adviser to the James Picker Foundation with respect to its Canadian program. Accordingly, if the proposed studies are to be carried out in Canada, requests for information and application forms should be directed to the Awards Office, National Research Council of Canada, Ottawa 2.

PUBLIC HEALTH SERVICE

Live Poliovirus Vaccine.—The Public Health Service's committee on live poliovirus vaccine, headed by Dr. Roderick Murray, chief of the division of biologics standards, reported three sets of attenuated poliovirus strains have been proposed for use as orally given vaccines. The strains developed by Dr. Albert Sabin of the University of Cincinnati have all had extensive field trials in eastern Europe, Mexico, and Singapore. The strains developed by Dr. Herald Cox of the Lederle Laboratories have been widely used in Latin America. The type 1 strain developed by Dr. Hilary Koprowski, Wistar Institutes, Philadelphia, has been used in a large trial in the Belgian Congo, but no significant amount of field information is available concerning Koprowski's type 2 strain, and only limited information is available in relation to his type 3 strain.

There is a marked difference in the neurovirulence of the three sets of strains as determined by intrathalamic and intraspinal inoculation in monkeys. On this basis, the Sabin group has an advantage over the others, but none of these strains is completely nonvirulent when inoculated intraspinally into monkeys. There is no evidence that any of these vaccines produced any harm to the persons to whom they were given. The thoroughness with which the observations were made varied in different studies. In some studies the ability of these strains to multiply and thus produce antibodies was less than could be expected on theoretical grounds. Apparently a number of factors operated in the field which might have prevented alimentary infection and the subsequent development of immunity.

A number of workers have reported that virus excreted by vaccinated persons showed increased neurovirulence for monkeys. There is much disagreement among investigators as to the significance of these reversions in virulence. Field experience with any strain to date does not afford reasonable proof that the community of nonvaccinated persons will be free of danger from possible reversion of virulence in excreted virus under a great variety of readily anticipated circumstances. This is one of the most important unresolved problems. Under some circumstances the simultaneous administration of all three types of virus may be effective.

The major problems to be solved before definitive decisions can be made regarding licensing include determining the significance of increased neurovirulence for monkeys of virus excreted by vaccinated persons, the demonstration of adequate measures of effectiveness of live poliovirus vaccines in field trials which, to be definitive, must involve large population groups, the development of standards to determine the possible presence or absence of contaminating agents in the vaccine, and the establishment of carefully designed and evaluated studies to demonstrate the production of specific antibodies in 90% or more of the susceptible persons inoculated in order to assure the potency.

Members of the committee, in addition to Dr. Murray, were Dr. David Bodian, professor and director, department of anatomy, Johns Hopkins University; Dr. William McD. Hammon, head, department of epidemiology and microbiology, Graduate School of Public Health, University of Pittsburgh; Dr. Alexander Langmuir, chief, epidemiology branch, the Public Health Service's Communicable Disease Center, Atlanta, Ga.; Dr. Joseph Melnick, professor of virology and epidemiology, chairman of department of epidemiology, College of Medicine, Baylor University; and Dr. John R. Paul, professor of preventive medicine, section of epidemiology and preventive medicine, School of Medicine, Yale University. Copies of the report are available on request.

Personal.—Dr. Stanton Garfield, fellowship program director and training officer in the division of international health, was retired, having reached the age of 64 years. He was responsible for planning training programs for foreign health and medical personnel in the United States under sponsorship of the International Cooperation Administration and the World Health Organization.

DEATHS

Alsobrook, Henry Bernis Ⓜ New Orleans; born in Manning, Ark., Feb. 26, 1893; Tulane University School of Medicine, New Orleans, 1923; formerly on the faculty of his alma mater; veteran of World War I; member of the Central Association of Obstetricians and Gynecologists; fellow of the American College of Surgeons; served as vice-president of the Louisiana State Medical Society; past-president of the New Orleans Gynecological and Obstetrical Society, Louisiana Obstetrical and Gynecological Society, and the Orleans Parish Medical Society, of which he was secretary; at one time secretary of the Louisiana State Gynecological Society; at various times on the staffs of the Mercy, Charity, and French hospitals; on the honorary staff and at one time president of the medical staff of the Southern Baptist Hospital, where he died July 28, aged 66.

Amelkin, Solomon Samuel Ⓜ Brooklyn; Long Island College Hospital, Brooklyn, 1925; associated with the Williamsburg General Hospital, where he was a founder and president; died in the Jewish Hospital Aug. 8, aged 57.

Baker, Charles Ⓜ West Milton, Ohio; Medical College of Ohio, Cincinnati, 1899; past-president of the Darke County Medical Society and the Miami County Medical Society; on the courtesy staffs of Miami Valley Hospital and Good Samaritan Hospital in Dayton, and the Stouder Memorial Hospital in Troy, where he died July 26, aged 86.

Barclay, Hugh Baily Ⓜ Greensburg, Pa.; Hahnemann Medical College and Hospital, Philadelphia, 1901; died July 29, aged 80.

Berghausen, Oscar Ⓜ Cincinnati, Ohio; Medical College of Ohio, Cincinnati, 1904; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; consulting physician at the Bethesda Hospital and Good Samaritan Hospital, where he died July 27, aged 80.

Berner, David A., Margate, N. J.; Medico-Chirurgical College of Philadelphia, 1901; past-president of the Atlantic County Medical Society; veteran of World War I; died July 29, aged 89.

Brown, Phebe Pamela Ⓜ Poughkeepsie, N. Y.; University of Buffalo School of Medicine, 1921; associated with St. Francis Hospital and Vassar Brothers Hospital, where she died July 23, aged 80.

Bruce, William H., Winston-Salem, N. C.; Leonard Medical School, Raleigh, 1907; associated with the Kate Bitting Reynolds Memorial Hospital; died July 24, aged 77.

Caldwell, Walter W., Kansas City, Mo.; Kansas Medical College, Medical Department of Washburn College, Topeka, Kan., 1906; died July 21, aged 81.

Capron, Manley Joseph Ⓜ Battle Creek, Mich.; University of Illinois College of Medicine, Chicago, 1916; fellow of the American College of Physicians; past-president of the Calhoun County Medical Society; veteran of World War II; associated with the Leila Y. Post Montgomery and Community hospitals; consultant in internal medicine at the Battle Creek Sanitarium, where he died July 26, aged 69.

Clayton, Herman C. Ⓜ Sidney, Ohio; Chicago College of Medicine and Surgery, 1917; veteran of World War I; served on the staff of the Memorial Hospital, Piqua; died July 29, aged 64.

Cochrane, Wayne Alexander Ⓜ Jackson, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1908; veteran of World War I; associated with the W. A. Foote Memorial Hospital, where he died July 31, aged 82.

Colomb, Brooks Amedee Ⓜ New Orleans; Tulane University School of Medicine, New Orleans, 1920; veteran of World Wars I and II; chief psychiatrist at the regional office of the Veterans Administration; died in Pass Christian, Miss., July 26, aged 61.

Crockett, Robert Newton Ⓜ Woodville, Miss.; Memphis (Tenn.) Hospital Medical College, 1911; served as health officer of Wilkinson County; died in the Field Community Hospital at Centreville July 26, aged 77.

Cummings, David Joseph Ⓜ Brownstown, Ind.; born May 6, 1878; Central College of Physicians and Surgeons, Indianapolis, 1901; past-president of the Jackson County Medical Society; named "Doctor of the Year" by the Indiana State Medical Association; veteran of World War I; served on the Selective Service Board of Jackson County during World War II; for many years county health officer; in 1954, in appreciation of more than 50 years service to the people of Brownstown and surrounding communities, a bronze plaque was presented to him; honorary president of the Jackson County Schneck Memorial Hospital Foundation and the Jackson County Schneck Memorial Hospital, Seymour, where he died July 26, aged 81.

Ⓜ Indicates Member of the American Medical Association.

Damon, Albert Hobart Ⓜ Limestone, Maine; University of Vermont College of Medicine, Burlington, 1900; veteran of World War I; served as health officer; chairman of the school board; honorary fire chief of Limestone; past-president of the Limestone Chamber of Commerce; died in the Community Hospital, Fort Fairfield, July 27, aged 87.

Dodge, J. G., Abilene, Texas; University of Louisville (Ky.) Medical Department, 1894; died in Sweetwater July 29, aged 90.

Eckdall, Frank Albert Ⓜ Emporia, Kan.; Rush Medical College, Chicago, 1901; also a pharmacist; past-president of the Lyon County Medical Society; for many years local surgeon for the Atchison, Topeka, and Santa Fe Railroad; served as vice-president of the American Association of Railway Surgeons; veteran of World War I; associated with St. Mary's Hospital and the Newman Memorial County Hospital, where he died July 31, aged 86.

Ecker, Lewis Charles Ⓜ Washington, D. C.; Syracuse University College of Medicine, 1906; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; served on the faculty of the Howard University College of Medicine and the Georgetown University School of Medicine; veteran of World War I; consultant emeritus, Washington Medical Center; died in Fayetteville, N. Y., Aug. 10, aged 76.

Edmunds, Page Ⓜ Gibson Island, Md.; University of Maryland School of Medicine, Baltimore, 1898; member of the founders group of the American Board of Surgery; for many years served on the faculty of his alma mater; fellow of the American College of Surgeons; veteran of World War I; formerly chief surgeon of the Baltimore and Ohio and the Washington, Baltimore and Annapolis railroads; died Aug. 7, aged 87.

Erlanger, Paul Simon Ⓜ Sarasota, Fla.; Eberhard–Karls–Universität Medizinische Fakultät, Tübingen, Württemberg, Germany, 1922; served a residency at the Monroe County Infirmary in Rochester, N. Y.; died July 20, aged 65.

Fernald, Fred Ⓜ Nottingham, N. H.; Baltimore Medical College, 1900; past-president and vice-president of the New Hampshire Medical Society; past-president of the Rockingham County Medical Society; member of the staff of the Exeter (N. H.) Hospital; for many years physician at the Rockingham County Home in Brentwood, where the Fernald Nursing Home was named in his honor; died July 17, aged 84.

Fielding, Bennett Irving Ⓜ Worcester, Mass.; Tufts College Medical School, Boston, 1921; president-elect of the Massachusetts Academy of General Practice; member of the American Academy of General Practice and past-president of the Worcester Chapter; formerly police surgeon; veteran of World War II; associated with the Fairlawn and Hahnemann hospitals, and St. Vincent Hospital, where he died July 30, aged 60.

Fisher, William Henry Ⓜ Centreville, Md.; University of Maryland School of Medicine, Baltimore, 1905; past-president of the Queen Annes County Medical Society; formerly county health officer: associated with the Memorial Hospital in Easton and the Kent–Queen Annes Hospital in Chestertown; died in the Peninsula General Hospital, Salisbury, Aug. 4, aged 78.

Fishman, C. J. Ⓜ Oklahoma City, Okla.; Rush Medical College, Chicago, 1908; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; past-president of the Oklahoma County Medical Society; professor emeritus of medicine at the University of Oklahoma School of Medicine; associated with Mercy, Wesley, and University hospitals, and St. Anthony Hospital, where he died July 26, aged 77.

Fordyce, Ora Otis, Coral Gables, Fla.; Ohio Medical University, Columbus, 1905; member of the American Psychiatric Association; for many years superintendent of the Toledo (Ohio) State Hospital; served as staff member and superintendent of the Athens (Ohio) State Hospital; died July 21, aged 82.

Fosse, Benjamin Ⓜ Beloit, Wis.; Northwestern University Medical School, Chicago, 1904; veteran of World War I; a member of the Beloit fire and police commission for 11 years, and its chairman for six years; served on the staff of the Beloit Hospital; died Aug. 2, aged 80.

Gamble, Eugene Beasley Ⓜ New Zion, S. C.; Medical College of South Carolina, Charleston, 1911; formerly member of the school board; on the staffs of the Clarendon Memorial Hospital in Manning and the Tuomey Hospital in Sumter, where he died July 22, aged 70.

Gittens, William W. Ⓜ McKeesport, Pa.; Howard University College of Medicine, Washington, D. C., 1911; associated with the McKeesport Hospital, where he died July 30, aged 78.

Gordon, Kenneth William Ⓜ Los Angeles; Baylor University College of Medicine, Dallas, 1930; served during World War II; died July 16, aged 70.

Gorham, Fordyce Clark, Seattle; University of Pennsylvania Department of Medicine, Philadelphia, 1899; died July 17, aged 90.

Grady, Edmund Mathias, Seattle; Creighton University School of Medicine, Omaha, 1933; interned at the Mercy Hospital in Council Bluffs; died July 31, aged 57.

Graham, George Warren, Collins, Iowa; Drake University College of Medicine, Des Moines, 1905; died in Charles City July 17, aged 80.

Hackler, Robert Hardin Jr. Ⓜ Washington, N. C.; Jefferson Medical College of Philadelphia, 1926; specialist certified by the American Board of Radiology, Inc.; member of the American Trudeau Society and the American College of Radiology; fellow of the American College of Physicians; associated with the Bertie County Memorial Hospital in Windsor, Martin General Hospital in Williamston, and the Tayloe Hospital; died in the North Carolina Memorial Hospital in Chapel Hill Aug. 4, aged 57.

Hall, LeGrande Larson Ⓜ Whittier, Calif.; University of Colorado School of Medicine, Denver, 1932; interned at the Charity Hospital in New Orleans and the Hospital of the Good Samaritan in Los Angeles; served a residency at San Francisco Hospital, where he was a fellow in urology, and Franklin Hospital in San Francisco; one of the founders and member of the board of directors of the Beverly Community Hospital in Montebello; associated with the Murphy Memorial and Presbyterian Intercommunity hospitals; died July 27, aged 53.

Hannabass, James W., Charles City, Va.; Medical College of Virginia, Richmond, 1914; died in Richmond July 28, aged 68.

Hemphill, Clyde Hoke Ⓜ Black Mountain, N. C.; University of Maryland School of Medicine, Baltimore, 1913; died July 17, aged 68.

Henshaw, John Cullen Ⓜ Warren, Ohio; Pulte Medical College, Homeopathic, Cincinnati, 1896; for many years county coroner; associated with the Trumbull Memorial Hospital; died July 23, aged 85.

Hunt, Kenneth Stovall Ⓜ Griffin, Ga.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; served as chairman of the Griffin–Spalding County Board of Education; member of the Southeastern Surgical Congress; fellow of the International College of Surgeons; elected Man of the Year in 1956 by the Griffin Exchange Club in recognition of his long and outstanding service and leadership in Griffin and Spalding County; veteran of World War I; died in St. Joseph's Hospital, Atlanta, July 28, aged 68.

Jackson, Dudley Ⓜ San Antonio, Texas; born in Eddy Aug. 26, 1890; University of Texas School of Medicine, Galveston, 1917; fellow of the International College of Surgeons and the American College of Surgeons; past-president of the Bexar County Medical Society; veteran of World War I; in 1955 the Dudley Jackson Fellowship in Malignant Disease at the University of Texas M.D. Anderson Hospital and Tumor Institute, Houston, was established in his honor; engaged in cancer research for many years, was active in legislative matters concerning cancer research and hospitals, and, with the late Congressman Maury Maverick, worked on the bill that led to the setting up of the National Cancer Institute; the American Cancer Society awarded him the bronze medal for outstanding contributions to the cause of cancer control; associated with the Robert B. Green Memorial Hospital and the Nix Memorial Hospital, where he died July 25, aged 68.

Jackson, John Andrew Crittenden, Lexington, Ky.; Howard University College of Medicine, Washington, D. C., 1925; died Aug. 5, aged 61.

Jamieson, James George Silver Ⓜ Portland, Maine; University of Edinburgh Faculty of Medicine, Scotland, 1902; died in Winchester, England, July 23, aged 83.

Jeffrey, Stewart Lee, Miami, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; on the staff of the Mercy Hospital; died July 21, aged 77.

Johnston, Robert Clarence Ⓜ New Kensington, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1901; fellow of the American College of Surgeons; associated with the Citizens General Hospital, where he died July 24, aged 85.

Kendall, Ellis A. Sr., Hot Springs National Park, Ark.; Meharry Medical College, Nashville, Tenn., 1902; died in Peoria, Ill., July 19, aged 82.

Kistler, Clinton J. Ⓜ Lehighton, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1895; for many years associated with the Palmerton (Pa.) Hospital; died in the Gnaden Huetten Memorial Hospital July 15, aged 87.

Koehler, Alfred Edward Ⓜ Santa Barbara, Calif.; Harvard Medical School, Boston, 1925; associated with Santa Barbara Cottage Hospital; died July 27, aged 62.

Kriete, Frederic Martin, San Francisco; born in Tokyo, Japan, Jan. 8, 1913; Rush Medical College, Chicago, 1938; interned at the University Hospitals in Iowa City; served a residency at the Presbyterian Hospital in Chicago, the University Hospitals in Cleveland, where he interned, and the City Hospital in Cleveland; specialist certified by the American Board of Preventive Medicine; in 1943 joined the Utah State Health Department and later served as chief of the division of maternal and child health; came to the California State Department of Public Health in 1947 as chief of maternal and child health, in 1950 became assistant chief of the division of preventive medical services, and in 1957 deputy state health director; died in the Mount Zion Hospital July 25, aged 46.

Lacey, Martin J. Ⓜ Albany, Calif.; Northwestern University Medical School, Chicago, 1911; veteran of World War I; served as health officer of Albany; part owner of the Taylor–Lacey Hospital in Auburn, Wash., until 1930; died July 22, aged 79.

Lang, George Washington Ⓜ Dormont, Pa.; University of Pittsburgh School of Medicine, 1910; past-president of the Allegheny County Medical Society; veteran of World War I; associated with the Elizabeth Steel Magee and St. Clair Memorial hospitals in Pittsburgh; died July 28, aged 71.

Link, Vaughen Harwood Ⓜ Hagerstown, Md.; Medical College of Virginia, Richmond, 1939; died in the Washington County Hospital July 26, aged 46.

Lipnik, Benjamin Philip Ⓜ Momence, Ill.; Chicago Medical School, 1942; veteran of World War II; member of the American Academy of General Practice; on the staff of St. Mary's Hospital in Kankakee, where he died July 30, aged 48.

Loyd, Oscar Howard Ⓜ Vega, Texas; Ensworth Medical College, St. Joseph, Mo., 1893; served as county health officer; died at the Northwest Texas Hospital in Amarillo July 21, aged 91.

McHugh, Thomas Jefferson Ⓜ Baton Rouge, La.; born in Zachary Oct. 16, 1890; Tulane University School of Medicine, New Orleans, 1914; member of the Southeastern Surgical Congress; past-president of the East Baton Rouge Medical Society; fellow of the American College of Surgeons; veteran of World War I; member of the medical advisory board for the Selective Service System during World War II; served as a member of the state board of examiners for practical nurses and as city health officer; associated with the Baton Rouge General Hospital and Our Lady of the Lake Sanatorium; died July 20, aged 68.

Mahoney, Andrew Walter, Providence, R. I.; Georgetown University School of Medicine, Washington, D. C., 1914; fellow of the American College of Surgeons; served as a medical officer with the British Army during World War I; for many years associated with St. Joseph's Hospital, where he died July 29, aged 66.

Mahrer, Herbert Albert, Cleveland; Western Reserve University School of Medicine, Cleveland, 1917; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; served as president of the Cleveland Radiological Society; consultant radiologist, for many years chief of the department of radiology, and for two years president of its medical council, Mount Sinai Hospital, where he died July 15, aged 66.

Markle, Louis, Inkster, Mich.; Vanderbilt University School of Medicine, Nashville, Tenn., 1915; died in Oak Park, Ill., Aug. 1, aged 68.

Mechling, Robert Steiner Ⓜ Pittsburgh; University of Michigan Medical School, Ann Arbor, 1943; interned at St. Francis Hospital; served a residency at the Presbyterian Hospital and the Pittsburgh Medical Center; specialist certified by the American Board of Surgery and the American Board of Proctology; fellow of the American College of Surgeons; veteran of World War II; instructor in proctology at the University of Pittsburgh School of Medicine; associated with the Veterans Administration, Presbyterian, Woman's, and Passavant hospitals; died at his summer home in Lancaster County, Va., Aug. 9, aged 42.

Melcher, Warren Coleman, Fayetteville, N. C.; Meharry Medical College, Nashville, Tenn., 1917; died July 23, aged 67.

Minnick, Robert Parks, Ordway, Colo.; Medical College of Virginia, Richmond, 1904; veteran of World War I; for four terms Montana state representative; formerly practiced in Saco, Mont., where he was for many years a member of the board of education; died in La Junta July 14, aged 80.

Mulherin, Hugh Gallagher, Mobile, Ala.; Medical College of Georgia, Augusta, 1929; died July 26, aged 56.

Nifong, Harry Davis Ⓜ Mansfield, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1904; for many years on the staff of the St. Joseph's Hospital in Fort Worth; died in the Mansfield Hospital Aug. 3, aged 76.

Nolan, William Patrick, Mebane, N. C.; University of Pittsburgh School of Medicine, 1913; served in France during World War I; died July 29, aged 72.

Norman, Estella Gertrude Ⓜ Davis City, Iowa; American Medical Missionary College, Battle Creek, Mich., 1907; fellow of the American College of Physicians; served on the staff of the Battle Creek (Mich.) Sanitarium and the Miami–Battle Creek Sanitarium in Miami Springs, Fla.; died in the Decatur County Hospital, Leon, July 26, aged 86.

North, William Boydston, Summit, N. J.; Toledo Medical College, 1901; died June 21, aged 81.

Northrup, Clarence Edgar Ⓜ McConnelsville, Ohio; Starling Medical College, Columbus, 1903; for many years health commissioner of Morgan County; served as secretary of the Morgan County Medical Society; medical examiner for the draft during World Wars I and II; died July 8, aged 79.

Nuzzi, Giovanni, Jersey City, N. J.; Regia Università di Napoli Facoltà di Medicina e Chirurgia, Italy, 1924; interned at the Mount Vernon Hospital in Mount Vernon, N. Y.; died July 3, aged 66.

Ohlmacher, Joseph Christian Ⓜ Vermillion, S. D.; born in Sycamore, Ill., Oct. 27, 1874; Rush Medical College, Chicago, 1901; instructor of pathology at Northwestern University Medical School in Chicago, 1901-1902; formerly dean and professor of pathology and bacteriology at the University of South Dakota School of Medical Sciences; at one time director of the state health laboratory; in 1954 was presented the Distinguished Service Award of the South Dakota State Medical Association, of which he was a past-president; served on the staffs of the Independence (Iowa) State Hospital and the Clarinda (Iowa) State Hospital; from 1952 to 1956 pathologist at St. Luke's Hospital in Aberdeen; died July 31, aged 84.

Pansing, Holley H., Dayton, Ohio; Medical College of Ohio, Cincinnati, 1905; for many years county health commissioner; served as president of the Ohio Federation of Public Health Officials; died July 27, aged 78.

Patterson, Lucius Kennedy Ⓜ Colonel, U. S. Army, retired, El Paso, Texas; born in Lumpkin, Ga., Oct. 7, 1893; Emory University School of Medicine, Atlanta, 1917; member of the American Academy of General Practice; entered in the medical corps of the U. S. Army in 1918; rose through the various ranks to that of colonel on Dec. 10, 1937; veteran of World Wars I and II; retired March 31, 1949; for recognition of his services in the Pacific, was awarded the Legion of Merit, Bronze Star and four campaign stars, denoting two years of overseas service; also was awarded World War I and pre-Pearl Harbor and Mediterranean ribbons; died in the William Beaumont Hospital July 17, aged 65.

Patterson, William Proudfit Ⓜ Fairchance, Pa.; Western Pennsylvania Medical College, Pittsburgh, 1905; veteran of World War I; died in the Uniontown (Pa.) Hospital July 30, aged 78.

Percoco, Michael, Mount Vernon, N. Y.; Regia Università degli Studi di Roma. Facoltà di Medicina e Chirurgia, Italy, 1934; on the staff of the Mount Vernon Hospital; died July 26, aged 52.

Pierson, Orra Atwood Ⓜ Woodward, Okla.; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1903; served as county health officer and coroner; associated with the Memorial Hospital; died July 31, aged 91.

Rapp, Albert Grant, Amityville, N. Y.; Cornell University Medical College, New York City, 1929; fellow of the American College of Surgeons; veteran of World War II; died July 30, aged 55.

Richard, Robert Edwin Ⓜ Prosser, Wash.; Georgetown University School of Medicine, Washington, D. C., 1953; member of the American Academy of General Practice; certified by the National Board of Medical Examiners; interned at the Kings County Hospital in Brooklyn; served a residency at the Sacred Heart Hospital in Spokane; chief of staff of Prosser Memorial Hospital; died in McConnellsburg, Pa., July 20, aged 34.

Ringena, Engelke Jansen Ⓜ Brooklyn, Iowa; State University of Iowa College of Medicine, Iowa City, 1908; for many years served on the board of education in Brooklyn; died in the Community Hospital, Grinnell, July 7, aged 81.

Samuels, Bernard Ⓜ New York City; born in Front Royal, Va., June 29, 1879; Jefferson Medical College of Philadelphia, 1907; specialist certified by the American Board of Ophthalmology; professor emeritus of clinical surgery (ophthalmology) at Cornell University Medical College, where he was appointed clinical instructor of ophthalmology in 1914, subsequently becoming assistant professor and professor; veteran of World War I; member of the American Academy of Ophthalmology and Otolaryngology, of which he was past first-vice-president; member of the American Ophthalmological Society and Association for Research in Ophthalmology; fellow of the International College of Surgeons and the American College of Surgeons; in 1954 president of the 17th International Congress of Ophthalmology in New York; an honorary member of the Irish, French, and German ophthalmological societies; in 1949 was elected to the executive committee of the National Society for the Prevention of Blindness; since 1942 consultant in ophthalmology at the New York Hospital, where for many years he was attending surgeon; associated with the New York Eye and Ear Infirmary; joint author with Dr. Adalbert Fuchs of "Clinical Pathology of the Eye"; died in Wiscasset, Maine, July 26, aged 80.

Samuelson, L. Gordon, St. Peter, Minn.; University of Minnesota Medical School, Minneapolis, 1931; veteran of World War II; certified by the National Board of Medical Examiners; formerly practiced in Mankato; in 1955 accepted an appointment with the Minnesota State Department of Public Welfare as physician and surgeon at the St. Peter State Hospital, where he was recently appointed psychiatrist; died July 16, aged 55.

Sanderson, Samuel Edward, Tacoma, Wash.; Detroit College of Medicine, 1896; died July 27, aged 86.

Schiff, Nathan Samuel, Woodmere, N. Y.; University of Illinois College of Medicine, Chicago, 1916; associated with the Bellevue, New York

Post-Graduate, and Mount Sinai hospitals in New York City; died in Helsinki, Finland, July 25, aged 69.

Senn Edward Waltham Ⓜ Owatonna, Minn.; Minneapolis College of Physicians and Surgeons, 1906; died in the Owatonna City Hospital July 18, aged 78.

Severance, Roscoe Dunham Ⓜ Syracuse, N. Y.; born in Savannah, April 22, 1897; Syracuse University College of Medicine, 1920; specialist certified by the American Board of Orthopaedic Surgery; member of the American Academy of Orthopaedic Surgeons; fellow of the American College of Surgeons, of which he was a governor; served as clinical professor of orthopedic surgery at the State University of New York Upstate Medical Center; associated with the Reconstruction Home in Ithaca and the Hospital of the Good Shepherd; past-president of the Syracuse Kiwanis Club, the YMCA, and the Syracuse University Medical Alumni Association; died in Clayton July 30, aged 62.

Shelby, Mitchell Hudson Ⓜ Cape Girardeau, Mo.; Vanderbilt University School of Medicine, Nashville, Tenn., 1914; served as secretary of the Cape Girardeau County Society for Crippled Children and Adults; associated with the St. Francis and Southeast Missouri hospitals; died July 29, aged 68.

Shinbach, Chester Coleman Ⓜ Columbus, Ohio; Ohio State University College of Medicine, Columbus, 1930; specialist certified by the American Board of Orthopaedic Surgery, Inc.; member of the American Academy of Orthopaedic Surgeons; instructor in surgery (orthopedic) at his alma mater; associated with the Grant and Children's hospitals; died July 30, aged 51.

Shull, Samuel David Ⓜ Chambersburg, Pa.; Medico-Chirurgical College of Philadelphia, 1908; also a pharmacist; for 24 years served as Franklin County coroner, retiring from that post in 1956; for 15 years examiner and medical adviser for the Selective Service; associated with the Chambersburg Hospital; a member and past-president of the Rotary Club; died in the Chambersburg Hospital July 21, aged 78.

Slack, James Aylmer Ⓜ Florence, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1905; veteran of World War I; died in the Eliza Coffee Memorial Hospital July 19, aged 76.

Slaughter, Guy Peter, Winslow, Ariz.; University of Nebraska College of Medicine, Omaha, 1937; interned at Bishop Clarkson Memorial Hospital in Omaha; served a residency at the City Hospital and University Hospital in Cleveland; in 1941 named field consultant to the Arkansas State Board of Health; veteran of World War II; died July 12, aged 47.

Sloan, Robert Ⓜ New Hartford, N. Y.; University and Bellevue Hospital Medical College, New York, 1913; past-president and treasurer of the Oneida County Medical Society; charter member of the Utica Academy of Medicine; served as chairman of the committee on maternal welfare in Oneida County, and for six years on the school board of Utica; for many years associated with St. Luke's and Faxton hospitals in Utica; died in the Oneida City Hospital, Oneida July 13, aged 67.

Smeltzer, Dave Harvey Ⓜ Charlotte, N. C.; Duke University School of Medicine, Durham, N. C., 1950; interned at the Charlotte Memorial Hospital, where he served a residency; veteran of World War II; member of the American Academy of General Practice; died in the Mercy Hospital July 22, aged 37.

Steinhardt, Ernest Henry Ⓜ Pueblo, Colo.; the Hahnemann Medical College and Hospital, Chicago, 1913; veteran of the Spanish-American War; retired plant physician for the Colorado Fuel & Iron Corporation; at one time on the staff of the Colorado State Hospital; died July 28, aged 82.

Sternberg, Joseph Edward Ⓜ Quincy, Mass.; Boston University School of Medicine, 1909; at one time on the staff of the Massachusetts Memorial Hospitals in Boston; died in Dennisport July 13, aged 85.

Stewart, Alexander, St. Paul, Minn.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1909; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; served in the medical corps of the Canadian Army during World War I; associated with Ancker, St. Luke's, Miller, and Children's hospitals; died in St. Joseph's Hospital July 23, aged 75.

Stewart, Thomas J., St. Louis; Meharry Medical College, Nashville, Tenn., 1904; died in Hollis, N. Y., July 17, aged 84.

Stiehl, Elmer Philip, Belleville, Ill.; Washington University School of Medicine, St. Louis, 1908; for many years county physician; served as district superintendent for the Illinois State Health Department; president of the Stiehl Drug Company; died July 25, aged 73.

Tribou, Howard Arthur Ⓜ Commander, U. S. Navy, retired, Rockport, Maine; Harvard Medical School, Boston, 1912; fellow of the American College of Surgeons; veteran of World War I; entered the U. S. Navy in 1912; retired on Feb. 1, 1941; died July 22, aged 74.

FOREIGN LETTERS

BRAZIL

Sterility.—Dr. C. A. Ferreira, of the Institute of Gynecology of the National Rio de Janeiro University (*An. brasil. ginec.* 48:23, 1959) studied a series of 722 sterile women. About 40% of the women had been married two to six years, 84 (11.6%) had been married twice, and 4 (0.5%) three times. The age of the women varied from 15 to 46 (average 28.1) years. The prognosis for treatment varied in inverse ratio to the age of the patient. Of the 722 women 357 (49.4%) had primary sterility, 280 (38.8%) secondary sterility, and 85 (11.8%) had repeated abortions. Huhner's test of 523 husbands gave satisfactory results in 329, poor results in 108, and negative results in 86. A spermatogram was made of 104 husbands and of these 55 gave normal results, 21 showed oligozoospermia, 2 necrozoospermia, and 26 azoospermia. The sterility in 102 cases was due to the husband, in 60 it was due to cervical diseases, in 25 to systemic conditions, in 126 to tubal affections, in 95 to ovarian diseases, in 80 to hormonal factors, and in about 160 to inflammatory processes. Of 164 women who were treated to correct the cause of the sterility, 24 (14.6%) became pregnant.

Acute Arterial Obstruction of Extremities.—Dr. H. M. Coelho and co-workers (*Rev. paulista med.* 54:167, 1959) reported a series of 20 acute vascular obstructive accidents. Only one similar case had been reported in Brazilian literature. Seven of their patients were men and 13 were women and their ages varied from 21 to 82 (average 42.5) years. Except for one case caused by a dissecting aneurysm of the aorta and another by arterial trauma (intra-arterial transfusion) all were caused by embolism. Among those with embolism there was a predominance of patients (seven) who had pure mitral stenosis with auricular fibrillation. In two of these the embolic accident was the reason the patient sought medical attention as the cardiac symptoms were minimal. In two patients the embolism occurred during mitral commissurotomy. According to the site, the 23 obstructions (three patients had more than one) were distributed as follows: axillary artery 4, brachial artery 3, bifurcation of the aorta 5, iliac artery 4, femoral artery 5, and popliteal artery 2.

Of the five patients operated on within less than eight hours of the onset of symptoms, one died of surgical shock two hours after the embolectomy, the other four having been successfully operated on with reestablishment of the arterial circulation. One of these patients was in good condition seven months after the aortic embolectomy, which was performed 10 hours after a mitral commissurotomy. One patient died of an intrapericardial dissecting aneurysm and cardiac tamponade just after the operation. One patient died 15 days after mitral commissurotomy but at autopsy the cause of death could not be determined. Another patient died suddenly six days after embolectomy, probably from cerebral embolism, as the postoperative anticoagulant treatment was inadequate. The authors concluded that the high case fatality rate (45%) was due to delayed recognition. They, therefore, stressed the importance of early diagnosis and treatment.

COLOMBIA

Malarial Hepatitis.—Dr. Peñuela and co-workers of Bogotá reported at the ninth Colombian Convention of Gastroenterology in Cúcuta in May a series of eight patients fulfilling the following criteria: blood smears were positive for one or more species of plasmodium, no antimalarial treatment had been used, and no other disease that could cause liver damage was present. Needle biopsy of the liver and liver function tests were performed on each patient. In every one of these the liver function tests were abnormal, and all the biopsy specimens revealed pathological impairment of the liver. The authors concluded that in malaria there is always liver involvement.

Primary Lymphosarcomas of the Digestive Tract.—At the same meeting, Drs. R. Gutiérrez and A. Parra of Bogotá reported on a series of 33 patients with primary lymphosarcomas of the digestive tract. The ratio of the incidence in men and women was 2:1 and it occurred chiefly in the fifth decade of life. The most frequent signs and symptoms were anemia, weight loss, and superficial adenopathies. Invasion of the digestive tract was manifested by abdominal pain (61%), palpable mass (50%), and nausea and vomiting (37%). Death was caused by cachexia, toxemia, or hemorrhage. The most useful diagnostic methods were biopsy of superficial lymph nodes, laparotomy with biopsy of abdominal organs, and radiologic study. Once the diagnosis was established the average survival was 11½ months.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Postgastrectomy Syndrome in Gastroduodenal Ulcers and Cancer.—At the same meeting, Dr. J. Valencia and C. E. Louis, of Caracas, Venezuela, reported a series of 500 patients on whom gastrectomy was performed because of cancer or peptic ulcers. Extensive subtotal gastrectomy (70% of the stomach) was recommended for treatment of gastric ulcers that did not heal after four to six weeks of medical treatment. Complicated or intractable duodenal ulcers should also be treated by extensive subtotal gastrectomy. Gastric cancers were not helped by subtotal or total gastrectomies and most of these patients died less than five years after operation. As surgery is the only treatment possible, the best operation is extensive subtotal gastrectomy with resection of the spleen and regional lymph nodes. The most adequate subtotal gastrectomy is that which eliminates completely the pyloric antrum and part of the fundus, leaving a short afferent loop by which the dumping syndrome is overcome. Since extensive subtotal gastrectomies have been used, postoperative peptic ulcers and their complications have been rare.

Strongyloidiasis.—At the same meeting, Dr. A. Rivas-Gómez of Caracas, Venezuela, reported a series of 52 patients infected with Strongyloides stercoralis. Of these 44 complained of abdominal pain, 39 of chronic diarrhea, and only 1 had a dysenteric syndrome. Abdominal pain was localized in the umbilical region in 20, but in only 13 was it localized in the epigastrium. The diagnosis was made by demonstrating motile larvae in the stools. Radiologic study of the intestinal tract was rewarding if attention was paid to hypotony and hypokinesis of the intestinal tract structure of the valvulae *conniventes*, fragmentation of the barium meal, especially in the jejunum, and the existence of segmentary stenosis of the small intestine. In 14 patients the radiologic findings were the same as those described in patients with intestinal malabsorption. Ulcerative rectocolitis occurred when the parasites invaded the colon and disappeared after treatment. Nine patients had duodenitis. With the use of chlorbetamide the author was able to clear 90% of his patients' stools of larvae.

DENMARK

Lupus Erythematosus Disseminatus.—Dr. J. Bichel and co-workers (*Ugeskrift for laeger*, June 11, 1959) studied a series of 17 patients with lupus erythematosus disseminatus. They paid special attention to the L. E. cell phenomenon. Typical L. E. cells were found in 14 of these patients but were absent in 274 serums of another 51 patients who had rheumatoid arthritis. In only two patients was the test positive in the absence of clinically well-defined lupus erythematosus disseminatus. With regard to the modern treatment of this disease with chloroquine or a steroid, no claim for a radical cure could be made, and it was uncertain to what extent they could prolong life, but all agreed that steroids had a striking and rapid effect on the acute manifestations of the disease, temporarily suppressing them completely. By shunting it out of a phase threatening life into a quiescent state, steroids could avert secondary infections and the sequels of prolonged fever. Of the patients in this series 13 were in a state of clinical remission when last seen. Eight of them continued to receive treatment with a steroid and chloroquine.

Imipramine for Depressions.—Drs. K. Fotel-Andersen and E. Geert-Jörgensen (*Ugeskrift for laeger*, July 9, 1959) used imipramine to treat 100 patients who had endogenous depression. Therapy started with 25 mg. twice daily with a gradual rise to a maximum of 300 mg. daily, then a daily reduction by 25 mg. so that in the course of 20 days a maintenance dosage of 25 mg., three or four times daily, was reached. The drug was given by intramuscular injection, by mouth, or by a combination of the two. The largest doses often provoked a sense of dryness in the mouth and severe sweating. Giddiness, lassitude, tremor of hands, and palpitation of the heart were also observed, and the risk of acute hallucinations seemed to rise with the age of the patient, but on the whole side-effects were rare and relatively unimportant. Sixty patients achieved a complete remission, and 17 were much improved. Treatment with this drug compared well with shock treatment.

Social Problems of Epilepsy.—While it is commonly assumed that 3.5 per thousand of a country's population are epileptics, Dr. E. Kiörboe (*Nordisk medicin*, June 11, 1959) found this to be an underestimate as far as Denmark is concerned, for with its population of 4,500,000 it has about 25,000 epileptics. In view of the effectiveness of the medical treatment of epilepsy, a reduction of this number might have been anticipated, but in 1935 only 811 epileptics were receiving pensions from the public authorities, whereas the corresponding figure for 1955 was 1,317. In other words, the epilepsy pensionable rate rose from 0.22 to 0.30 per thousand between these two years, yet the ratio of epilepsy to other pensionable ailments remained constant during the same period, being 2.5%.

One reason the success of medical treatment was not better reflected in statistics is that the average life of epileptics has been prolonged. Again the psychic deterioration to which an epileptic may have succumbed is but little influenced by modern drugs. To be sure the epileptic is no longer so heavily drugged into apathy by bromides and other depressants, but, while modern drugs achieve the suppression of actual attacks of epilepsy, they often fail to cure its mental ill-effects. Epileptic attacks were the cause of only 18 of the 12,000 traffic and similar accidents dealt with by the Odense General Hospital in 1954. Kiörboe concluded that in Denmark the gravely afflicted epileptic is well cared for, and the lightly afflicted patient can well care for himself, whereas the intermediate group is still in great difficulty in a modern community in which there is less and less room for the worker who is slow to adjust himself to the quickened rhythm of the mechanical age.

Sanatorium Treatment of Neuroses.—In 1951 the Montebello Sanatorium was opened for the treatment of various neuroses, care being taken to scrutinize the applications for admission carefully to avoid blocking entry to it by a long waiting list. Even so, the average wait has been about two months. Dr. T. Østergaard (*Nordisk medicin,* June 11, 1959) studied the results achieved by occupational therapy and psychotherapy in the first two years of the existence of this institution. About 67% of the 1,059 patients treated and discharged were women, and most of them were comparatively young, only 16 being over 60 years of age. On discharge 45% were much improved, and 41% were moderately improved. A follow-up questionnaire was sent in 1955 to the 911 patients who were improved and was answered by 748 of them; 531 or 71% reported lasting improvement. In the remaining 29% there had been no improvement or it had been transient. The results were slightly better for the men than for the women. Heredity and environment did not have the deleterious effects anticipated, but the frequency of good results fell with the duration of illness, those faring best whose illness had lasted less than three years.

Renal Tuberculosis.—Drs. E. Halkier and J. Meyer (*Danish Medical Bulletin,* June, 1959) treated 90 patients who had renal tuberculosis with dihydrostreptomycin, para-aminosalicylic acid, and isoniazid. After six months of this treatment 82 patients had ceased to discharge tubercle bacilli in the urine. Of the remaining eight patients, three required nephrectomy. The authors concluded that six months of this triple treatment is sufficient to effect a cure in the overwhelming majority of patients in whom renal tissue is still intact, but to this generalization must be added the admonition that physicians or departments intending to undertake the treatment of renal tuberculosis must consider beforehand whether they have at their disposal the necessary knowledge, patience, and laboratory facilities for the control which is required over the years.

FRANCE

Appendix Graft in Replacement of the Ureter.—At the meeting in April of the Academy of Surgery, Dr. Kuss and co-workers presented the case of a 29-year-old man, the lumbar portion of whose ureter was resected by accident during the course of a sympathectomy performed because of arteritis. The authors used the appendix to form a graft, and an end-to-end anastomosis was performed. The urography performed six months after the operation showed a well-functioning kidney. It is still too early to forecast the future of the graft. The choice of the appendix as a graft of the ureter seems to be unique.

Arterial Changes in Atherosclerosis.—J. Loeper measured the potassium and silicon levels in normal and atheromatous arteries (*Information médicale et paramédicale,* April 7, 1959). The value of the silicon in normal arteries was 8 mg.% in infants and 6 mg.% in adults. In atherosclerosis there was a decrease in the content of silicon which dropped 2.2%. This decrease was marked even in moderately severe lesions. There was a parallel between the importance of the lesions and the percentage of silicon. Conversely, between the lipid overloading and the fall in silicon there was a decline too marked for an even minimal lipid overload. The calcium content, at the same time, increased. The potassium level in the arch of the aorta in normal subjects averaged 35 mg.%. This value decreased in atherosclerotic patients, but the decrease was not too great for a moderate lipid infiltration. On the other hand, it did not occur as early as the decrease of the silicon in the elastic fibers. The author believed that impairment of the elastic arterial tissue is an early lesion that may condition the appearance of atherosclerosis, which is not the simple mechanical consequence of subendothelial lipid infiltration.

Etheromania.—Prof. H. Desoille (*Encyclopédie Médico-chirurgicale*) stated that etheromania is observed mainly in perverse, intensely withdrawn subjects. The dose of ether inhaled or ingested may reach one liter per day. This type of intoxication is characterized by sudden onset and rapid disappearance. Thus, several bouts a day are possible. It appears in a form characterized by motor excitement and aggressiveness which may be erotic and an ecstatic form which may be associated with hallucinations, paresthesias, and eroticism. The acute intoxication may result in epileptiform seizures without the aura. Death is possible during one of these bouts. Subacute intoxication reminds one of the delirium tremens of alcoholics except that, while the latter is overcome by fear, the etheromaniac is aggressive. Other complications such as the impulse to set fire, to break, and to kill are common. The treatment requires admission to a health center. The withdrawal is facilitated by the absence of a state of need but the recovery from this toxicomania remains uncertain because of underlying personality defects.

Psychoanalysis and Automobile Accidents.—R. Held (*Ouest médical,* April 25, 1959) stated that the tense driver uses his automobile to satisfy his aggressive impulses or to express his guilt feelings. This tendency, most marked in the obsessed, exists also in normal subjects and explains some otherwise unexplainable behavior. A similar aggressiveness becomes manifest in pedestrians at road crossings because of a feeling of defiance toward the drivers in order to show whose is the right of precedence. Badly integrated aggressiveness constitutes the most frequent motivation. It manifests itself either against someone else, against vehicles being driven, or against the driver himself.

INDIA

Mental Health.—Speakers at a symposium agreed on the need for a mental health service with regional branches. There are few mental hospitals in the country and many are remodeled jails, a fact about which one psychiatrist has complained. Dr. H. Richards of the World Health Organization said that no new discovery can reduce the importance of sympathetic understanding of the mental patient. The emphasis in any mental health service should be on prevention and early treatment. Outpatient mental care should be widespread. Dr. S. Datta-Ray said that the proposed mental health service need not be based on the Western pattern, where the emphasis is on bigger hospitals. Recent medical discoveries have reduced the patient's period of hospitalization. He suggested that psychiatric clinics be attached to all large general hospitals.

Goiter Control.—Two field survey units of the Ministry of Health are engaged in delimiting the areas of goiter endemicity. The ministry hopes to determine the magnitude of the problem, supply iodized salt to inhabitants of the areas chiefly affected, and evaluate the results of iodine prophylaxis. Only iodized salt will be made available in the endemic areas. The price will be the same as that for ordinary salt. The cost of iodization will be met by the government. The United Nations International Children's Emergency Fund (UNICEF) will provide an iodization plant capable of processing 70 tons of salt per day or enough for a population of 2,750,000. The UNICEF will also lend two of its vehicles for the survey teams. The World Health Organization will furnish technical advice and guidance. Endemic goiter associated with cretinism, deaf-mutism, and various other grades of physical and mental deterioration is prevalent in some regions of India. About 9 million persons are affected with goiter in India.

Hereditary Spherocytosis.—Chatterjea and Ray reported a series of seven patients with hereditary spherocytosis (*J. Indian M. A.* 33:1 [July 1] 1959). This condition is very rare. The age of these patients varied from 2½ to 26 years. The onset of symptoms was insidious, with weakness, pallor, anemia, jaundice, and splenomegaly. Symptoms were present for one to five years before the patients sought treatment. Two had had three or four attacks of fever which was irregular and lasted for about a week. In one patient the diagnosis was made during a "crisis." He had an associated vascular pseudohemophilia and a deficiency of antihemophilic globulin factor. Two patients who complained chiefly of fatigability and weakness of four to five years' duration were found to have spherocytosis during family study. They also had attacks of epistaxis due to vascular pseudohemophilia. All except two had jaundice. Splenomegaly and hepatomegaly were present in all. Leg ulcers or enlarged lymph nodes were not found in any patient.

The hemoglobin level varied from 5.8 to 12.76 Gm. per 100 ml., the packed cell volume (PCV) from 17 to 38%, the mean corpuscular volume from 97 to 113, and the mean corpuscular hemoglobin concentration from 30 to 38%. The reticulocyte counts were 2.5 to 25.0% and the total white blood cell counts ranged from 5,400 to 15,300 per cubic millimeter. A variable number of the characteristic microspherocytes were present in the peripheral blood in all patients along with large-sized erythrocytes which thus showed a two-cell type population. A few immature cells were found in two patients with moderate anemia. Platelet counts were within normal limits. The osmotic fragility of the red blood cells was increased in all patients. Mechanical fragility was increased in some. Fetal hemoglobin level was raised in one patient only. The plasma hemoglobin level was normal, results of Coombs' test were negative, and cold agglutination titers were normal in all patients. Paper electrophoresis of hemoglobin showed a normal pattern.

Examination of the marrow revealed hypercellularity with normoblastic hyperplasia in four patients and a normal myelogram in one. In three patients with a history of epistaxis and bleeding from the gums, the bleeding time was prolonged and the plasma prothrombin level was normal. Prothrombin consumption was depressed in one patient. Roentgenograms of the skull and long bones showed generalized mottling of the skull ond osteoporosis in the hand. Cholecystograms in two patients showed no abnormality. Family study was made of available parents, siblings, and other close relatives.

The father of one patient showed a significant number of spherocytes in peripheral blood with increased osmotic fragility of the erythrocytes. Similar findings were obtained in the father and brother of another patient. Three other patients were brothers. Their father's blood showed spherocytes and increased osmotic fragility of the erythrocytes, and their mother had a history of epistaxis and menorrhagia but no spherocytes. The mother of the sixth patient and father of the seventh had spherocytes and increased osmotic fragility of the erythrocytes. Splenectomy was performed on two patients with good immediate response. Hemoglobin level and PCV increased and normal blood findings were still present nine months after operation. Reticulocytes and plasma bilirubin attained normal values in both but the spherocytes persisted.

SWEDEN

Serum Haptoglobin.—In the *Scandinavian Journal of Clinical and Laboratory Investigation* ([supp. 1] 11:169, 1959) Margareta Nyman reported on some aspects of the variation in the concentration of haptoglobin, the globin-binding serum protein fraction. A new electrophoretic method for determining haptoglobin based on direct determination of hemoglobin-binding capacity of the serum (HbBC) at physiologic pH was introduced. In serums from 277 normal blood donors the haptoglobin concentration was found to vary between 28 and 192 mg. per 100 ml., while no appreciable fluctuation was found in the individual haptoglobin level of healthy subjects. The findings of a significantly higher haptoglobin level in males than in females could be explained by the observation that administration of androgens increased and administration of estrogens decreased the haptoglobin concentration. Variations in the haptoglobin level during the menstrual cycle seemed to be negatively correlated with the estrogen content of the blood. As a rule haptoglobin could not be demonstrated in serums from newborn infants but appeared to reach normal concentration within a month. No systematic variation in HbBC was found with age.

Venesection and subsequent increase of erythropoiesis did not appear to influence the serum haptoglobin level. The haptoglobin level rose rapidly in conditions with inflammatory reactions and/or fever. The fact that an increase in the haptoglobin level was observed eight hours after injection of dead Escherichia coli appeared to suggest that connective tissue damage with or without an inflammatory reaction was not the only factor capable of stimulating haptoglobin synthesis. There appeared to be a striking similarity between the metabolism of fibrinogen and haptoglobin in acute infections.

Analysis of a series of patients with carcinoma without other diseases or treatment showed both high and normal haptoglobin values. Aseptic inflammatory reactions in connection with carcinoma increased the haptoglobin response. Haptoglobin determinations proved to be of limited value in the differentiation between hepatocellular and biliary tract disease. It was apparent from the results that in chronic as well as in acute hepatocellular failure the concentration of the circulating haptoglobin was, as a rule, depressed. A certain correlation was found between the haptoglobin level, the degree of splenomegaly, and the carbon monoxide hemoglobin concentration in the blood which supported the view that the depressed haptoglobin level was due at least in part to an increased hemoglobin catabolism.

An increased estrogen content in the blood and possibly partial degradation of haptoglobin owing to liver cell failure might contribute to the decrease observed in the HbBC. The possibility of a negative correlation between the haptoglobin level and the degree of fibrinolysis was suggested by the results of an analysis of the mononucleosis series. The author concluded that the determination of the haptoglobin level was of value as a general test for the presence of active disease, in the investigation of hematologic disorders, and as supplementary information in the differential diagnosis of hepatobiliary disease.

Diabetes.—Nils Törnblom (*Acta med. scandinav.* 164:23-37, 1959) gave 2, 2-bis [illegible], 1-dichloroethane (DDD) to [illegible]s who had hyperpolysaccharidemia and signs of hyaline vascular changes in the kidneys, with the object of reducing adrenocortical function and of lowering the serum polysaccharide level. Two of those whose renal injuries were already grave when DDD administration was begun died within a year. Medication had to be discontinued in one because it made the patient retch. For the remaining nine patients the percentage reduction in the number of eosinophil granulocytes following ACTH administration diminished during DDD medication indicating that the latter affected the adrenal cortex. The serum hyperpolysaccharidemia was markedly reduced. Impairment of visual acuity occurred in most of the patients. The inulin and para-aminohippuric acid clearances remained unchanged for 18 months and then declined slightly. A few patients felt nauseated after taking DDD. No other side-effects were observed. Signs of serious hepatic damage were not seen.

Cardiac Patients and Pregnancy.—Hjördis Robbe (*Acta obst. et gynec. scandinav.* 38:1-61, 1959) examined 28 women who had different types of heart disease, during pregnancy, labor, the puerperium, and about eight months after delivery. During pregnancy the total blood volume and total hemoglobin showed the same mean increases as in normal pregnant women. Four weeks after delivery stationary and normal values were found. The mean hemoglobin concentration was normal during and after pregnancy. The increase in heart volume measured radiographically was slightly, but not significantly, greater in the cardiac patients than in normal women. After delivery the heart volume of the cardiac patients diminished more slowly than that of normal women and stationary values were not found until several months after delivery.

The physical working capacity in the groups of patients with septal defects, pulmonary stenosis, and aortic vascular disease remained nearly constant during and after pregnancy except in two patients who had toxemia. In those with mitral valvular disease alone or combined with aortic valvular disease there was a higher mean pulse-rate response to any particular work load during pregnancy as compared with that in the nonpregnant state thus implying a diminished physical working capacity during pregnancy in these patients. The author concluded that in addition to the usual clinical examination of the cardiac patient during pregnancy serial examinations of the working capacity, blood volume, and heart volume were of practical diagnostic and prognostic value.

Injury to Ureters and Bladder in Gynecologic Surgery.—Accidental injuries of the ureters and the bladder are the most distressing complications of gynecologic operations. Bentsson and Ingemansson (*Acta obst. et gynec. scandinav.* 38:68-81, 1959) reported that of 5,400 major operations performed at the Women's Clinic of the Sabbatsberg Hospital in Stockholm 25 primary injuries of the bladder were recognized. This was an incidence of 0.5%. All of these injuries were treated by primary suture and all healed without complication. To decrease the incidence of ureteral injuries in gynecologic operations the most important measure is a careful dissection.

In hysterectomy it is advisable to separate the bladder from the cervix in an early stage of the operation and simultaneously to prepare the parametrial vessels, pushing the ureters laterally. In difficult adnexal operations it is well to make a peritoneal incision over the iliac vessels craniad to the adnexal tumor. In this situation the ureter would be easily recognizable and might be followed down to the critical point in the operation. As a preventive measure ureteral catheterization might be used but it is often hard to know when an operation will be technically difficult. The method has certain drawbacks such as ureteral bleeding, infection, and sometimes the impossibility of inserting the catheter if far advanced gynecologic tumors are present. The authors concluded that the repair of the ureter in their series had been successful when the implantation of the ureter was performed with Boeminghaus' technique and in patients in whom the bladder flap technique was used.

Abortion After Amputation of Cervix.—In operations for uterine prolapse the cervix is routinely amputated to minimize the risk of recurrence. Sven Svennerud (*Acta obst. et gynec. scandinav.* [supp. 1] 38:105-107, 1959) studied a series of 539 patients who were operated on for uterine prolapse. Of these patients 151 were still in the childbearing age at the time of the operation and 15 became pregnant (total 24 pregnancies). In one of these the cervix had not been amputated which gave a total of 14 patients in whom this operation had been performed. Only 40% of the pregnancies went to term and 44% terminated in abortion or premature birth. The risk of abortion after amputation of the cervix was thus found to be over four times as high as in a normal series.

Housewife's Eczema.—Erik Skog (*Nord. med.* 61:961-963 [June 25] 1959) studied 182 cases of housewife's eczema, of which 73% were considered to be toxic contact dermatitis and the rest allergic contact dermatitis. In all instances the sites involved were the hands and/or forearms. The initial lesions were most frequently noted on the fingers, especially under the wedding ring (34 patients). In most patients the onset was between the ages of 30 and 50 years. In those with allergic contact dermatitis the number of positive patch tests was highest for nickel sulfate, hand lotions, turpentine, formalin, and potassium bichromate. In the subjects sensitive to nickel it was found that in more than half the dermatitis had started under clasps containing nickel. The toxic contact dermatitis was considered to be caused by washing powders and detergents, mostly by their enhancement of the irritating effect of other commonly used household substances, such as solvents, floor polish, shoe polish, fish, meat, and fruit juices.

Dysmenorrhea and Absenteeism.—Sven Svennerud (*Acta obst. et gynec. scandinav.* [supp. 2] 38:1-116, 1959) studied a series of 890 working women aged 14 to 44 years. Dysmenorrhea was noted in 30.9%. In 16.8% it was nondisabling, in 8.3% it was sometimes disabling, and 5.8% it was regularly disabling. In a further 7.4% previous dysmenorrhea had ceased before the year of the investigation. Dysmenorrhea was most common (46.3%) in the 20-to-24-year age group. In that group the menstrual pain was sometimes disabling in 15% and regularly disabling in 8.9%. After 25 years of age the frequency of dysmenorrhea decreased rapidly and more rapidly among the married women. In about 11% dysmenorrhea was secondary to pelvic changes. The frequency of dysmenorrhea was not found to be influenced by environmental or emotional factors but was the same in such widely different occupations as factory workers, actresses, and athletes.

Dysmenorrhea often disappeared after pregnancy, independent of such factors as civil status and the result of the pregnancy. Factory workers were away from work on an average 28.8 days a year for all causes. The corresponding figure for office workers was 10.6. Absence because of dysmenorrhea represented only 1.1 and 0.3 days respectively. Total absence including absence because of illness varied to some extent with age but to a much greater extent with civil status, the married women being away from work about 10 days per year more than the unmarried women. Absence because of dysmenorrhea accounted for 3.7% of the total absence for factory workers and 2.5% for office workers and was not greater than absence without permission.

Children of Mothers Aged 42 and Over.—In a sample of 1,030 mothers aged 42 and over the total incidence of malformations among the children was 4.5%, as reported by Lindsten and Hagert (*Nord. med.* 61:753-756 [May 14] 1959). In this series were 9 pairs of twins and 1 set of triplets, a total of 1,041 children. In a total of 47 malformations, there were 22 cases of mongolism. The incidence of malformations was 45.1 per 1,000 births for mothers over 42 years of age, as compared to 13.4 for mothers of all ages. No influence of parity and age of the father could be demonstrated.

Pelvic Arteriography in Tubal Pregnancy.—Hüsnü Özaras (*Acta radiol.* 51:257-265 [April] 1959) studied a series of 37 women with tubal pregnancy. The duration of the pregnancy calculated from the first day of the last menstrual period varied between 35 and 210 days. In 26 of the 37 women with tubal pregnancy the uterine artery on the side of the affected tube was seen to give off one or more adnexal branches. Adnexal branches of the contralateral uterine artery were identified in 14 of these patients. In 20 of the 26 patients in whom adnexal branches of the uterine artery on the side of the affected tube were visible they were seen to divide into several branches. In 11 of these they were found to be arched. On the other side the adnexal branches were observed to ramify in rare exceptions only, and in none were they found to be arched.

Placental sinuses were filled with a contrast medium in 28 patients. In 26 they were seen to lie outside the uterus; in 11 patients draining veins were seen to arise from the placenta; in 3 of them the veins filled early in the arterial phase which suggested the presence of arteriovenous fistulas; and in the remainder they filled late or after the arterial phase. In 3 of the 37 patients with tubal pregnancy a corpus luteum of pregnancy was identified on the side of the nonaffected tube. In two the blood supply of the latter was derived from one ovarian artery. The author concluded that the demonstration of placental sinuses outside the uterus was proof of ectopic pregnancy. The differential diagnosis from intrauterine pregnancy might be difficult because the corpus luteum of pregnancy might occasionally be visible outside the uterus and might then be confused with ectopic pregnancy. Familiarity with these arteriographic appearances will aid in correctly differentiating between the two conditions.

Lidocaine for Epilepsy.—The effect of intravenous injections of lidocaine on patients with epileptic seizures, mainly grand mal and jacksonian attacks, was studied in a series of 52 patients of whom 27 were admitted with a diagnosis of cerebral tumor, 18 of epilepsy, 6 of acute brain damage, and 1 of acute encephalitis, by Einar Bohm (*Nord. med.* 61:885-889 [June 11] 1959). Lidocaine without epinephrine was given either in a single injection or by intravenous drip. Those seizures that responded to treatment ceased immediately after the injection without any influence on the degree of the patient's wakefulness. Of 12 grand mal attacks in seven patients 11 were arrested with a single dose of lidocaine ranging from 0.5 to 3 mg. per kilogram of body weight.

In 15 attacks of status epilepticus of the grand mal type in 12 patients lidocaine was given in doses between 2 and 10 mg. per kilogram of body weight. Complete relief was obtained in seven patients. Smaller doses produced only partial relief. In two patients who received 8 mg. per kilogram of body weight the attacks occurred early in the postoperative course after extirpation of a brain tumor. In these patients only partial relief was obtained. Both patients had postoperative hematomas. Since treatment with lidocaine had no hypnotic effect the diagnosis could be made early. At reoperation cerebral edema with cerebromalacia was present in the operative area. The failure of obtaining relief in these patients might have been due to the fact that the lidocaine did not reach the brain structures concerned in sufficient concentration because of impaired circulation as a result of the increased intracranial pressure, or because of a local circulatory disturbance in the operative area.

The 36 jacksonian attacks in 27 patients were treated with intravenous injections of lidocaine in doses ranging from 1 to 10 mg. per kilogram of body weight. Of these, 26 attacks were arrested with doses ranging between 1 and 5 mg. per kilogram of body weight. The 11 attacks that were not stopped occurred in four patients. In one patient in this series the convulsions were aggravated after injection of 2 mg. of lidocaine per kilogram of body weight. This patient had a glioma of the pons. In 23 attacks of status epilepticus of the jacksonian type in 21 patients lidocaine was given continuously in doses ranging from 1 to 10 mg. per kilogram of body weight. A blocking effect was obtained in 14 attacks with doses between 6 and 8 mg. per kilogram of body weight. Smaller doses produced partial relief. Two patients who received 8 and 10 mg. per kilogram of body weight an hour, respectively, without relief had postoperative hematomas. In some patients with myoclonic epilepsy and continuing local motor seizures administration of lidocaine had no influence on the convulsions. The site of action of lidocaine was presumed to be on a cortical level.

UNITED KINGDOM

Printing Strike Ends.—During the printing strike, which ended after seven weeks, the *British Medical Journal* (BMJ) appeared every week with the help of nonunion printers. The strikers paraded with placards asking doctors to boycott the BMJ. Some of them followed a van carrying journal sheets to a binding shop, which they put out of action. This caused a delay in publication, but did not prevent it, as the entire staff cooperated and worked 12 hours a day helping to produce the journal. Dr. Clegg, the editor, stated that he ruined two pairs of trousers in the cause and that the business manager singed his eyebrows in the printing foundry. At the beginning of the strike the BMJ committee considered getting the journal printed abroad as the *Lancet* did. This was printed in Germany and later in Paris, although in a much abbreviated form. The BMJ's usual printers at St. Albans refused to print the journal in spite of Dr. Clegg's plea that the weekly publication of the journal was essential for the health of the nation.

Printers not in the union who were willing to produce the BMJ were eventually found just outside London. Dr. Clegg called the secretary of one of the printing unions, who had declared in public that the printing of matters vital to health did not come under the ban of the strike, to see if he could help. The secretary said that as the journal was already being handled by nonunion labor his men could not possibly consider printing it. Although the BMJ appeared every week during the strike many difficulties were experienced. Distribution was delayed and vans containing printed sheets, galleys of type, and journal covers had to travel devious routes to avoid pursuing pickets.

Abdominal Decompression in Labor.—A chance observation has resulted in a new technique that shortens the first stage of labor. During an investigation of the source of electrical potential in labor, Heyns paralyzed the abdominal muscles with the relaxant succinylcholine and observed that the first stage of labor was surprisingly shortened (*J. Obst. Gynaec. Brit. Emp.* 66:220, 1959). He concluded that the uterus contracted more efficiently because it was no longer constricted by the tense abdominal wall. It assumed the mechanically favorable spheroid shape without the additional energy of overcoming the resistance of the abdominal muscles. Heyns then used an alternative method of relaxing the abdominal muscles by reducing the atmospheric pressure on the abdomen. Tests in a decompression chamber showed that pressure could be lowered without undue discomfort to the mother. Of 100 primigravida patients in whom decompression was begun early in labor, 50 became fully dilated in less than five hours, and 68 were delivered in less than seven hours from the time decompression was applied. In a second trial using improved apparatus 72% of the women were delivered within five hours of starting decompression.

Not only was labor accelerated, but pain, particularly backache, was relieved. This was demonstrated by comparing successive contractions with and without decompression. There was some mild respiratory discomfort, but this was compensated by the relief of pain. The tendency for the membranes to rupture later than normally in patients treated by decompression suggested that it produced a lower intrauterine pressure. This should diminish the chance of fetal compression and asphyxia. Another advantage of this method is that it gives the uterus more freedom to adjust its axis and improve the direction of the fetal head toward the pelvic brim—an advantage when the fetus is in the posterior position or when there is a high angle of inclination of the pelvic brim, and the axis of the inlet is so divergent from the axis of the uterus that much effort is expended in forcing the presenting part against the symphysis pubis. With this method, delivery occurred with the patient in the semireclining position, with flexed hips, which gave a mechanical advantage in making the axes of inlet and uterus more nearly parallel. An increase in frequency, strength, and duration of contractions was also noted. In one 25-year-old primigravida the cervix advanced from one finger to full dilatation after 24 contractions lasting 90 minutes.

The decompression equipment consists of a special semireclining chair, a plastic airtight suit, a rigid "spacer" to determine the area over which decompression is applied, and a decompression pump. The woman sits in the chair, the spacer is placed over the abdomen and the suit wrapped round like a sleeping bag, enveloping the patient from the axilla downward. She controls the pressure herself with her finger on an air-inlet valve leading to the pump. She closes the valve at the beginning of a contraction and releases it as the pain subsides. The obstetrician or midwife has access to the abdomen for auscultation of the fetus and to observe the progress of labor by means of a zip fastener in the front of the suit. When the second stage ends decompression is stopped and the patient is then delivered in the normal manner.

Heyns also observed the effect of decompressing the pelvic outlet by sitting the patient on decompression equipment during the second and third stages of labor. He claims that the fetus is delivered by primary uterine forces without the necessity for bearing down and that the placenta is expelled without pressure on the fundus of the uterus through the abdomen.

Status Epilepticus.—Evanson (*Lancet* 2:72, 1959) treated a 9-year-old boy who had status epilepticus with the muscle relaxant succinylcholine, and artificial respiration after other methods of treatment had failed. The patient was admitted to a neurosurgical unit for craniotomy, which revealed intracerebral, frontal, and parietal abscesses. These were aspirated and the cavities filled with penicillin suspension. Eighteen days later the boy developed status epilepticus, which failed to respond in turn to soluble phenobarbital injections, intramuscular injections of paraldehyde, and procaine and thialbarbital administered intravenously. It was then decided to give 50 mg. of succinylcholine and artificial respiration with an intermittent positive-pressure artificial respirator. This produced striking improvement, with return of color and blood pressure to normal. Thereafter 50 mg. of the relaxant was given every 15 to 20 minutes, and artificial respiration was maintained to give adequate pulmonary ventilation. A further operation was then performed to irrigate the cortex.

After the operation whenever attempts were made to withdraw the muscle relaxant convulsions returned with respiratory embarrassment and cyanosis. Administration was therefore continued intravenously at a rate of 50 mg. every 15 to 20 minutes for about eight hours. Attacks became less frequent and diphenylhydantoin was given by a gastric tube. Six weeks later the patient was well, the only after-effects being slight dysphasia and a right facial paresis. Evanson recommended this treatment for status epilepticus to prevent anoxic brain damage when the usual anticonvulsants, barbiturates, and paraldehyde have failed.

Inhibition of Intrinsic Factor.—A technique for the detection of blocking antibodies to Castle's intrinsic factor was devised by Taylor, who used it to show that the serum of some patients with pernicious anemia contains another factor that inhibits this factor (*Lancet* 2:106, 1959). Tests of the absorption of vitamin B_{12} labeled with radioactive cobalt (Co^{60}) were made using the fecal excretion method. A standard test dose of 0.5 mcg. of Co^{60}-vitamin B_{12} was used, either alone or with 50 mg. of a preparation of hog intrinsic factor which was made up in 10 ml. of distilled water and kept overnight at 4 C before use. Immediately before administration 45 to 55 ml. of human serum was added, and the mixture given with the test dose of vitamin B_{12}. The serums were obtained from healthy persons and patients with pernicious anemia who were untreated or whose disease was in remission.

It was found that the serums from a number of patients with pernicious anemia inhibited intrinsic factor activity, and it was considered that this might be due to an immune response. Three patients whose serums had been shown to be markedly inhibitory were treated with 80 mg. of hydrocortisone daily for a month, and treatment parenterally with vitamin B_{12} was continued during this time. This caused the inhibitory effect on intrinsic factor activity to be greatly reduced, although the capacity to absorb vitamin B_{12} was not increased. This suggested that a true antibody might be involved. It is possible that some autoimmune process may occur in those patients with pernicious anemia whose serum inhibited intrinsic factor activity.

Hazards of Hair Sprays.—The increasing use of cosmetics has created new medical problems because some of the constituents used in their manufacture are potentially toxic. Hair sprays have now come into the category of hazardous aids to beauty, despite careful directions for their application. Edelston (*Lancet* 2:112, 1959) described the case of a young woman whose lungs were affected by the continual inhalation of a hair spray. She was referred to the hospital by her doctor with a history of cough, malaise, and loss of appetite and energy of one year's duration. On questioning she admitted spraying her hair twice daily for six months with two well-known brands of hair fixative. Physical examination revealed no abnormality.

A roentgenogram of the chest showed bilateral hilar adenopathy and diffuse mottling mainly confined to the middle and lower zones of both lungs. The lung lesions were attributed to the continual inhalation of the hair spray, the synthetic resins of which are known to produce granulomas of the lungs. These resins include polymers of polyvinyl alcohol and polyvinyl pyrrolidone. They are not metabolized, but the particles are phagocytosed by the cells of the reticuloendothelial system and can be demonstrated in the liver, spleen, lungs, and other organs, where they lodge and produce granulomatous reactions. Polyvinyl pyrrolidone is carcinogenic in mice and rats. After the use of the spray had been discontinued, radiologic studies of this woman showed a gradual resolution of the hilar adenopathy and the reticular lesions in the lungs.

CORRESPONDENCE

PATIENTS REFERRED FOR CHECKUP

To the Editor:—The article by Cohen, entitled "Hypokalemic Muscle Paralysis Associated with Administration of Chlorothiazide," in The Journal, Aug. 22, page 2083, has great teaching value. Since it reports a case of iatrogenic suffering, it appears to be worthwhile to look into the background. It appears that an obese 60-year-old man had his eyes examined. The ophthalmologist told him that there were signs of high blood pressure in his eyes and sent him to an internist, who did not find anything significant except the fact that the patient was overweight and had a blood pressure of 180/124 mm. Hg.

This initial blood pressure reading did not mean anything because the patient had already been "scared to death" by one or two doctors. He was given a diet, which he did not follow, and chlorothiazide therapy. He soon gained 11 lb. (5.0 kg.), which proved that he was not overweight because of fluid retention or congestive failure but that obviously he was a problem eater, who used large quantities of food to quiet his jangling nerves. His chlorothiazide intake was increased; he was given amphetamine; and apparently he was reprimanded about his diet. His weight and blood pressure started to drop, and he became so sick that he had to be hospitalized. He was then given a complete series of tests, including serum-potassium level determination, which would have done more good if done prior to the use of such powerful drugs. It turned out that if he had stopped taking medicaments and had started drinking 1 qt. of orange juice daily he would have been all right. It is hoped that his doctor, who was an instructor in medicine, lost some of his therapeutic ardor.

The treating of patients who are referred to the internist by ophthalmologists and optometrists is a problem that needs more attention. Arteriosclerotic changes in the eye do not necessarily indicate generalized arteriosclerosis. Hypertensive changes are often transient. Degenerative changes that interfere with vision are annoying and are often aggravated by measures designed to lower the blood pressure. Patients with such changes often go from one ophthalmologist to another, get numerous minor changes in their eyeglasses, and end up with a drawer full of glasses, all of them more or less alike and rather expensive. If they are lucky they eventually find an ophthalmologist or an internist who is both mature and kind, who will not say that the symptoms are due to age and that nothing can be done, but who will give them hope and long-term treatment which will make them feel that something is being done for them. Use of one of the newer cholesterol solvents is likely to help.

Although several good articles along these lines have been published, antihypertensive therapy has been greatly overworked. For every patient with malignant hypertension we see 10 patients who suffer from the side-effects of antihypertensive therapy. It would be helpful if we could have an article by one of our senior teachers on the treatment of patients who are referred for a general checkup because of abnormal ocular findings.

Ralph W. Ballin, M.D.
62 Greene St.
Cumberland, Md.

PROBLEMS OF IMPAIRED SPEECH

To the Editor:—The editorial entitled "Problems of Impaired Speech and Language," in The Journal, Aug. 22, page 2102, presents an excellent summary of the present status and knowledge of organic speech disorders. However, I would like to point out that the reference to the situational disorder of stuttering presents only one viewpoint of this rather controversial subject. The statement that "Considerable research to date provides no appreciable support for the hypothesis that stuttering is characteristically associated with or symptomatic of severe emotional disturbance or neurosis in a clinically significant sense" is of extreme dubiety for the very reason that psychiatric research which might be construed as relating to this hypothesis is extremely sparse. The dismissal of this hypothesis because of the extremely superficial research which has been performed to date could only be regarded as highly illogical. However attractive this rejection may be to the average speech therapist and especially to those who themselves have a problem with, or a background of, stuttering, I think that any impartial observer in the field will agree that psychiatric investigation of individual stutterers and their background has often shown a substratum of emotional maladjustment that is antecedent to, and apart from, the social manifestations of the speech disorder itself.

Jesse R. Freeland, M.D.
508 16th St.
Oakland, Calif.

MISCELLANY

MEDICAL NUMISMATICS—PHYSICIANS PORTRAYED ON COINS AND CURRENCY

Roy J. Popkin, M.D., Los Angeles

The monetary system of a nation is one of its most cherished possessions. Great pride is taken in maintaining its stability and strict laws protect it from debasement or counterfeiting. In contrast to postage stamps which are changed often and honor innumerable persons, only a nation's most famous or distinguished citizens are acknowledged by having their portraits on coins or currency. In some countries, such as England, the reigning monarch is the sole person portrayed. In the United States, only the most famous statesmen are portrayed on coins or currency. In the early history of the United States, the regular coinage often bore such symbolic figures as Liberty, an Indian, or an eagle. For a time after the Civil War, many generals, cabinet members, and local political figures were honored. Scientists, religious leaders, explorers, musicians, and other distinguished citizens have been acclaimed throughout the world on regular or commemorative issues. In the United States, commemorative coins, chiefly half dollars honoring historical persons, places, and things have been issued from 1892 through 1954. The first United States commemorative coin portrayed Columbus and was issued for the Columbus Exposition in Chicago. The last was issued in 1954 commemorating Booker T. Washington and George Washington Carver.

One would assume that physicians would be frequently honored for their medical achievements or contributions to the welfare of mankind. However, since the time of the ancient Greeks and Romans who revered Hippocrates and Galen, no physician has been given such a tribute for his purely medical contributions for over 1,500 years. In contrast, many physicians have been paid such a tribute on postage stamps. Over 500 different stamps have been issued by almost every modern country recognizing physicians, but only three have been distinguished in modern times for their purely medical contributions by having their portraits on coins or currency.

The Republic of Austria was the first nation since the time of the ancient Greeks and Romans to acclaim a physician for his medical accomplishments only. Austria honored Dr. Theodor Billroth in 1929 on its commemorative two-schilling coin and Dr. Julius Wagner-Jauregg was honored on its regular 500-schilling note in 1953. The only other nation to pay homage to a physician in this manner was Brazil, which recognized Dr. Oswaldo Cruz on its regular 400-reis coin issued from 1936 through 1938.

Only four other physicians have been acclaimed and these solely for their achievements in the political field. The United States commemorated Dr. John McLoughlin. Dr. Jose Rizal was honored by the Philippine government. The Republic of China honored Dr. Sun Yat-Sen, and the Republic of Lithuania honored Dr. Jonas Basanavicius.

Physicians Honored for Medical Achievements

Biographical sketches of the physicians honored for their medical achievements and examples of the coins and currency are as follows:

Christian Albert Theodor Billroth, M.D.—Dr. Christian Albert Theodor Billroth, more widely known as Theodor Billroth, was the first physician to be honored by any nation or people in modern times for his purely medical achievements. He was of Swedish origin and was born in Bergen on the island of Rügen in 1829. He died in Austria, his adopted country, in 1894. He obtained his medical degree at the University of Berlin in 1852. After extensive postgraduate work he returned to become *Privat-Dozent* in surgery. In 1860 he accepted the professorship of surgery at Zurich and in 1867 he accepted the same position at Vienna, where he spent the remainder of his professional life. His "General Surgical Pathology and Therapeutics" was published in 1863 and immediately established him as a great teacher. This work was quickly translated into numerous languages, including Russian and Japanese, and went through many editions. He was one of the most distinguished practicing surgeons of his day. He worked and wrote extensively. In 1887 he was honored by being chosen a member of the Austrian Imperial Chamber of Lords.

Dr. Billroth was also a great student of music and the psychology of music and, in addition, was an accomplished musician. He played the first violin and second violin parts in a string quartet which met at his home for years. He was an intimate friend and admirer of Brahms and many of Brahms' works were privately performed at Billroth's home before they were published. His work on the psychology of music was published after his death.

Dr. Billroth was honored by the Austrian Republic on the centenary of his birth. His portrait was placed on the two-schilling commemorative silver coin (fig. 1) of 1929.

Oswaldo Cruz, M.D.—Dr. Oswaldo Cruz, Brazil's great physician and scientist, was born in San Luis, Brazil, in 1872 and died in 1917. He received his medical degree from the University at Rio de Janeiro and later studied at the Pasteur Institute and Toxicology Laboratory in Paris. He was an outstanding worker in tropical diseases and his contributions to bacteriology are many. He was director of public health of Rio de Janeiro and was directly responsible for eliminating yellow fever from the city. His efforts in reforming the Brazilian Sanitary Service resulted in not only a nationwide decrease in yellow fever but also a decrease in plague, malaria, and smallpox as well. He was an untiring worker in the improvement of sanitation. He described the trypanosomiasis which now bears his name.

He founded an institute of bacteriology and serum therapy in Rio de Janeiro which was later given the name of Cruz Institute. From this institute have emanated numerous investigations of insects, parasites, and reptiles.

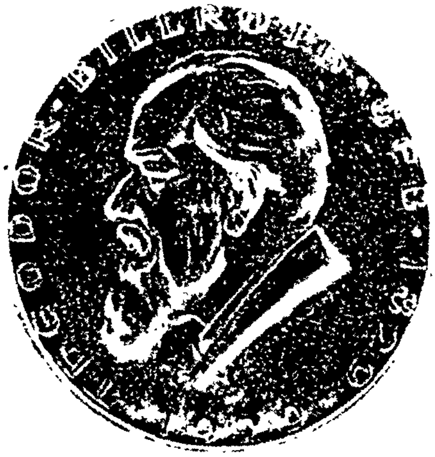

Fig. 1.—Two-schilling, silver, commemorative coin of the Republic of Austria, issued in 1929.

Dr. Cruz was the second physician honored in modern times by any nation or people for only his medical accomplishments. The Brazilian government issued a 400-reis copper-nickel coin (fig. 2) on which was emblazoned the portrait of Dr. Cruz. These coins were minted in 1936, 1937, and 1938.

Julius Wagner-Jauregg, M.D.—Dr. Julius Wagner von Jauregg was born in Austria in 1857 and died in 1940. He dropped the von and substituted the hyphen in his name shortly after World War I when the governing political party at the time frowned on any distinction of nobility. He obtained his medical degree in 1880 from the University of Vienna, where he began his career in the department of experimental pathology and internal medicine. In 1883 he joined the staff of the psychiatric clinic. He later accepted the position of professor of psychology and neurology at the University of Graz (Austria). He published extensively in psychiatry, physiology, and pharmacology. His first malaria inoculations for dementia paralytica were started in 1917. This work led to his receiving the Nobel prize in medicine in 1927, for the malaria therapy of general paresis.

The Republic of Austria honored Dr. Wagner-Jauregg in 1953 by placing his portrait on the 500-schilling note (fig. 3). Dr. Wagner-Jauregg's honor is more distinctive as he is the only physician ever honored on currency for contributions of a medical nature.

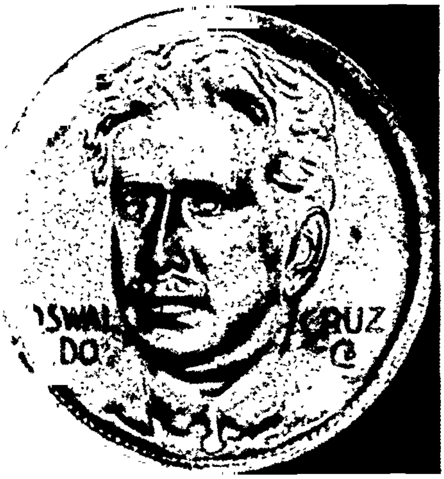

Fig. 2.—Four-hundred reis, copper-nickel coin, regular coinage of Brazil, issued in 1936.

Physicians Honored for Nonmedical Achievements

The following biographical sketches are of the physicians honored for their achievements other than medical, with examples of the coins and currency.

Dr. John McLoughlin.—Dr. John McLoughlin is the only physician to be honored in the United States by having his portrait on its money. Dr. McLoughlin was born in Canada in 1784 and died in Oregon in 1857. He obtained a good general education in Canada and Scotland. In 1824 he was sent as the Chief Factor for the Hudson's Bay Company for the territory west of the Rocky Mountains and which he governed for 22 years. He built Fort Vancouver on the northern bank of the Columbia River in 1825. This later became the city of

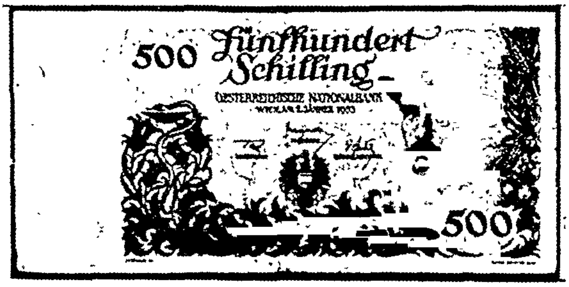

Fig. 3.—Five-hundred schilling banknote of the Republic of Austria. The face bears Dr. Wagner-Jauregg's portrait, his name, the dates 1857-1940 and on the left the healing serpent of Aesculapius.

Vancouver, Wash. He also founded Oregon City. He governed the entire northwest region, which was to comprise the states of Idaho, Washington, and Oregon. He was a strong and capable leader.

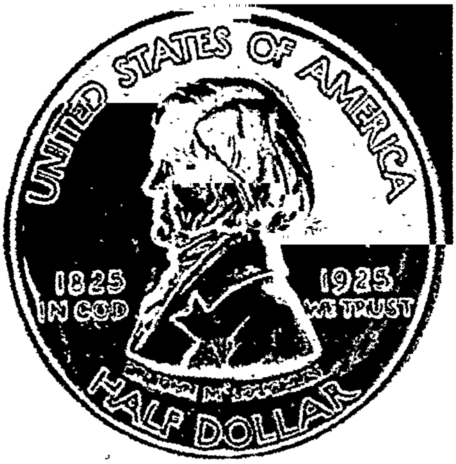

Fig. 4.—Half dollar, commemorative coin of the United States, issued in 1925.

He opened the country to the settlers and smoothed the way for missionaries. Through his efforts, a war between the United States and Great Britain was averted. Shortly after he assumed his duties as Chief Factor, he became known as Dr. McLoughlin. Although he had no formal medical training, he administered to the white and Indian population and apparently was a skillful and resourceful physician. He was called "the father of Oregon" by the Americans and the "great white chief" by the Indians.

Dr. McLoughlin's portrait appears on the 1925 Fort Vancouver Centennial half-dollar (fig. 4) of the United States. The coin commemorates his founding of the city of Vancouver, Wash.

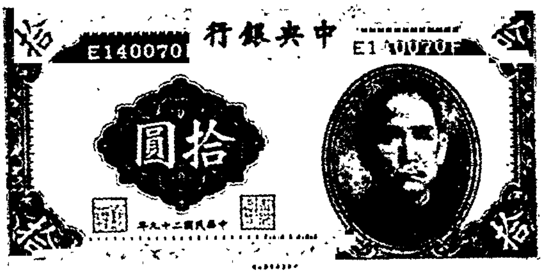

Fig. 5.—Dr. Sun Yat-Sen's portrait on the 10-yuan note, issued by Central Bank of China in 1940. Dr. Sun Yat-Sen was honored also on the one-yen silver dollar minted in 1912.

Sun Yat-Sen, M.D.—Dr. Sun Yat-Sen, Chinese Republican leader, also known as the father of the Chinese Republic, was born in 1867 and died in 1925. Dr. Sun Yat-Sen obtained his medical degree from the Hongkong Medical School in 1894. He was the leader of the movement which overthrew the Manchu government and on Jan. 5, 1912, he became the first president of the New Republic of China. He was a strong advocate of Western ideas and attempted many reforms. His political career fluctuated widely, although his influence in the government continued great.

His portrait appears on numerous denominations of coins and currency (fig. 5) issued by the Chinese Republic and various Chinese banks from 1912 until 1947.

Jose Rizal, M.D.—Dr. Jose Rizal was a great Filipino patriot who was born in 1861 and died by execution before a Spanish firing squad for his political activities in 1896. He studied medicine in Manila and later was graduated from the University of Madrid where he received the M.D. and Ph.D. degrees. He studied in the great medical centers of Europe and was elected a member of the Berlin Anthropological Society. He then returned to the Philippines but soon left as he could not tolerate the Spanish rule. He lived in Japan, various cities in North America, and later London. He wrote on many subjects and his works included a political novel. He was back home when a native insurrection broke out. The Spanish authorities tried him as the instigator. He was condemned and shot.

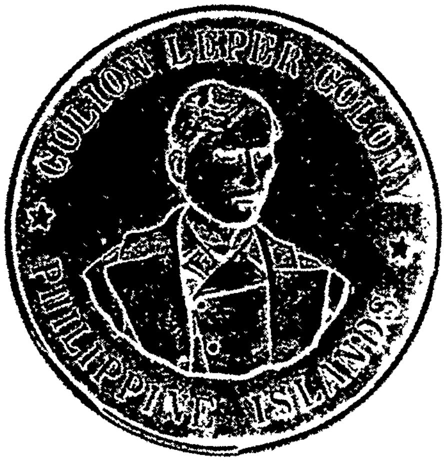

Fig. 6.—Culion Leper Colony, one of the few official coinages issued by a medical organization, issued by the Philippine Health Service for use in Culion Leper Colony and leper stations. Dr. Rizal was honored as a patriot and not as a physician. The coin is one peso, dated 1925, and is nickel-bronze.

Dr. Rizal is held in great esteem by the Filipino people. A province in the island of Luzon was named after him. He was honored in 1920 and in later years by having his portrait on the Culion Leper Colony coins of one peso (fig. 6) and lesser denominations. His portrait also appears on the two-peso currency note issued before World War II. The same denomination overprinted on the back with the word "victory" was reissued after the liberation of the Philippines from Japanese occupation. After the postwar period, the note (fig. 7) was printed without the "victory."

Jonas Basanavicius, M.D.—Dr. Jonas Basanavicius, the Lithuanian physician, scholar, and statesman was born in 1851 and died in 1927. He obtained his medical degree at the University of Moscow. Early in his career he practiced medicine in East Prussia, where he edited the famous Lithuanian nationalistic journal *Ausra* or *Dawn*. Lithuania was an unwilling part of Imperial Russia at the time and was struggling against Russian rule. The journal printed in the Lithuanian language was smuggled into Lithuania. In 1885, Dr. Basanavicius was obliged to leave Germany because of this political activity; later for many years he practiced medicine in Bulgaria. In 1905 after the Russian revolution, the Congress of Vilna under his presidency demanded autonomy for Lithuania. As the revolution failed, the demands of the congress were unheeded. Dr. Basanavicius was equally famous as a scholar and was especially interested in Lithuanian folklore, for which he has been styled the patriarch of the Lithuanian renaissance.

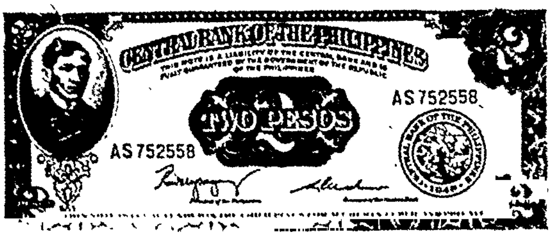

Fig. 7.—Two-peso bank-note, which was in circulation prior to the Japanese invasion, also honoring Dr. Rizal.

After the Russian revolution in 1918, Lithuania proclaimed its independence. Dr. Basanavicius wrote its constitution and was active in its affairs. He was founder and president of the Lithuanian Scientific Association.

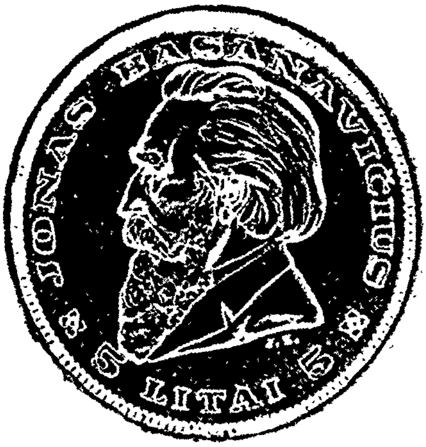

Fig. 8.—Five-litai silver coin of Lithuania minted in 1936 and 1937, bearing the portrait of Jonas Basanavicius.

He was honored by having his portrait on the five-litai silver coin (fig. 8) issued in 1936 and 1937. Lithuania was incorporated into the U. S. S. R. in 1940 and its coinage became obsolete.

When one considers the numbers of political, military, and religious leaders, explorers, pioneers, scientists, and musicians among many others honored on their nation's coins or currency, the few physicians so esteemed is pitifully small.

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THE CHEMISTRY OF HEREDITY

Reprinted with permission from S. Zamenhof, Hereditary Defects in Man, Springfield, Ill., Charles C Thomas, Publisher, 1959.—Ed.

HEREDITARY DEFECTS IN MAN

Name of Disease	*Biochemical Symptoms*
Albinism	Failure to manufacture melanin
Alkaptonuria	Failure to oxidize homogentisic acid
Cystinuria	Abnormal excretion of cystine, lysine, arginine and ornithine; urinary calculi
Galactosemia	Failure to convert galactose-1-phosphate into glucose-1-phosphate
Gaucher's disease	Deposition of abnormal amounts of kerasin in the cells of reticuloendothelial system
Glycogenosis	Accumulation of glycogen in the liver, heart and spleen
Gout	Elevated blood uric acid and deposition of sodium biurate in the tissues
Hemolytic anemia (spherocytosis)	Defect in glycolysis
Hemophilia	Missing blood clotting factor
Hypercholesterolemia	Elevated blood cholesterol
Hypophosphatasia	Abnormal mineralization of bone; diminished alkaline phosphatase activity; increased urinary excretion of phosphatidylethanolamine
Infantile amaurotic idiocy	Accumulation of sphingomyelin in the brain cells
Pentosuria	Excretion of pentose sugars in the urine
Phenylketonuria	Failure to convert phenylalanine to tyrosine
Porphyria	Excretion of the porphyrins in the urine and feces
Sporadic cretinism with goiter	Defective synthesis of thyroid hormone
Tyroketonuria	Failure to convert p-hydroxyphenylpyruvic acid into 2,5-dihydroxyphenylpyruvic acid
Wilson's disease	Defective copper metabolism

MEDICAL LITERATURE ABSTRACTS

SURGERY

Total Gastrectomy. P. Chrysopathis, V. Golematis and M. Sakai. J. Internat. Coll. Surgeons 32:17-23 (July) 1959 [Chicago].

The authors report on 22 patients with gastric carcinoma in whom total gastrectomy was performed. In all patients total gastrectomy was combined with splenectomy and partial left pancreatectomy. The 22 patients were divided into 2 groups. Group A included 14 patients. In 6 of these, adenocarcinoma of the cardia involved the lower part of the esophagus, the cardioesophageal lymph nodes, and the lymph nodes of the hilus of the spleen. In 8 patients the growth involved the body of the stomach. The abdominal approach was employed in 9 patients and the thoracoabdominal in the other 5. In 7 of the 14 patients the continuity of the alimentary tract was reestablished by the Roux en-Y anastomosis, and in the remaining 7 by end-to-side esophagojejunostomy according to Braun's method. Two patients in this group died from peritonitis, which occurred as a result of leakage of the anastomosis. Group B included 2 patients in whom the tumor was situated at the cardia and 6 patients in whom the growth involved the body of the stomach and the prepyloric region, with metastasis to the regional lymph nodes. The thoracoabdominal approach was employed in 1 patient and the abdominal in the remaining 7. The continuity of the alimentary tract in these 8 patients was restored by interposition of an intestinal segment, 15 to 20 cm. long, between the esophagus and the duodenum. The upper end of the isolated jejunum was anastomosed end-to-side with the loop. This loop was anastomosed end-to-end with the duodenum. The authors compared the operative methods used in the 2 groups and came to the conclusion that the restoration of the alimentary tract by interposition of an intestinal loop between the esophagus and the duodenum is the method to be preferred. The reasons are as follows: 1. It is well supported by the patient. 2. The esophagojejunal anastomosis is safer. 3. The creation of a loop on the isolated segment of jejunum acts as a gastric reservoir for food. 4. The interposition of the intestinal loop maintains normal passage of the food through the duodenum. 5. Regurgitation of bile and the dumping syndrome are eliminated, judging from the results in this series.

Lipoma of the Colon: With Report of Seven Cases. W. A. Nelson and J. V. Rogers Jr. South. M. J. 52:767-773 (July) 1959 [Birmingham, Ala.].

The authors report on 7 patients (3 men and 4 women) with lipoma of the colon who had been seen at the Emory University Hospital between 1949 and 1958. The ages of the patients ranged from 48 to 69 years. Although 50% of the previously reported cases of lipoma have occurred in the cecum and ascending colon, all 7 lipomas were situated in the distal half of the colon. Diagnosis was established by radiographic findings in 3 cases, and it is believed that the diagnosis would be strongly suspected today with the authors' present knowledge of this condition in 2 additional cases. Three of the 7 patients had gastrointestinal bleeding, 4 complained of constipation of a significant degree, and only 1 had diarrhea which alternated with constipation. Five patients had lower abdominal pain, and 1 patient had intussusception. Two patients expelled the lipoma spontaneously prior to surgical intervention. In 1 case ulceration of the tumor was reported by the pathologist. In 2 cases the pathological report failed to state whether or not ulceration was present, although both of the patients had significant rectal bleeding. Four of the lipomas were pedunculated. It is suggested that the presence of intussusception in an adult should make one suspect the possibility of a lipoma of the colon.

Enzymatic Débridement with Bovine Fibrinolysin. W. W. Coon, E. F. Wolfman Jr., J. A. Foote and P. E. Hodgson. Am. J. Surg. 98:4-8 (July) 1959 [New York].

Enzymatic débridement is a feasible and rational adjunct to the treatment of infected wounds. Fibrinolysin and desoxyribonuclease extracted in noncrystalline form from bovine pancreas were used by the authors in the treatment of 50 patients with chronic ulcerating lesions of the skin. Eight patients presented abscess cavities and infective operative wounds; 6 wounds were uncomplicated by osteo-

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The place of publication of the periodical appears in brackets preceding each abstract.

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myelitis and 3 of them healed by secondary intention while under treatment with fibrinolysin and desoxyribonuclease. A clean granulating base developed in the other 3 wounds which were closed successfully by excision and primary closure in 2 instances and by split-thickness skin grafting in the other. Complete healing was not attained in the remaining 2 wounds which were associated with osteomyelitis. Sixteen patients presented ulcerations associated with arteriosclerotic peripheral vascular insufficiency. Six ulcers failed to show significant improvement; 7 were satisfactorily débrided, but subsequent healing did not occur. Three ulcers improved markedly, 2 were in diabetics with peripheral arterial disease in whom trauma and infection may have been more important than a decrease in arterial blood supply. The remaining 2 ulcers were successfully grafted with split-thickness skin after fibrinolysin débridement for 4 and 6 days respectively. Débridement was effective in 3 patients with trophic ulcers. Considerable improvement was obtained after 3 to 6 days of treatment with fibrinolysin in 6 patients with decubitus ulcers which had failed to respond to weeks of treatment with saline and hydrogen peroxide soaks. Four patients with stasis ulcers showed rapid and marked improvement with 1 to 9 days' enzymatic débridement. A fifth similar ulcer which had been present for 9 years showed no improvement after 5 days of fibrinolysin therapy. Good results were obtained in patients with chronically infected second and third degree burns. Side-reactions or irritations were not noticed. All the ulcerations selected for this study had failed to respond, even after weeks, to the usual conservative measures of saline, hydrogen peroxide, or acid soaks. The poorest over-all response to fibrinolysin was seen in patients with lesions complicated by underlying arterial insufficiency. The authors point out that optimal results can be expected in those patients with simple infected wounds or ulcers uncomplicated by arterial insufficiency, radiation change, large amounts of dead collagenous tissue, or dense scar. In these instances, one can expect almost uniformly rapid and effective preparation of the wound for grafting, secondary closure, or spontaneous epithelization. Except in deep, irregular abscess cavities, the preparation of choice will probably prove to be a combination of fibrinolysin and desoxyribonuclease in a water-miscible ointment base.

Control of Nasal-Staphylococcal-Carrier States. H. J. Weinstein. New England J. Med. 260:1308-1310 (June 25) 1959 [Boston].

This report is based on a study carried out in the surgical section of a large tuberculosis hospital in which the staphylococcic-nasal-carrier state in all personnel assigned to the surgical services was studied as part of an extensive program of infection control. All were required to have nose and throat cultures at regular intervals. In the presence of negative nose and throat cultures, reculture was carried out every 6 weeks. Those with positive throat but negative nose cultures were included in the 6-week schedule, and those with positive nose cultures were admitted to a double-blind study to evaluate the efficacy of topical antibiotics in eliminating carrier states. A preparation consisting of bacitracin ointment, U. S. P., containing 500 units of bacitracin per gram, to which was added 5 mg. of neomycin per gram, was used for treatment. An identical preparation, consisting only of the petrolatum base, was used as a placebo.

Of 110 persons, who submitted 606 nose cultures during the observation period, 39% were found to be nasal carriers of hemolytic coagulase-positive Staphylococcus aureus. Treatment with bacitracin-neomycin ointment resulted in negative cultures in 72% of those treated, as compared to the group treated only with placebo ointment, in whom cultures became negative in only 23%. In a control group receiving no treatment whatsoever, cultures became negative in 22%. The reduction of the carrier rate by about 80% suggests the possibility of significantly reducing this one source of cross infection.

Stretching of the Sciatic Nerve: A Means of Relieving Postoperative Pain Following Removal of Ruptured Lumbar Intervertebral Discs. J. E. Adams and V. T. Inman. California Med. 91:24-26 (July) 1959 [San Francisco].

Stretching the sciatic nerve for the relief of "sciatica" was frequently employed before 1900 and was subsequently abandoned, probably because it was done without sufficient scrutiny of the indications. The authors present a 37-year-old woman who had been subjected to conservative and surgical treatment for recurrent severe lumbar and sciatic pain. In view of the fact that the patient had no pain while quiet and recumbent but did have severe pain in the leg when she moved either the back or the leg in any way that caused movement of the sciatic nerve roots, the authors reasoned that if the nerve root could be stretched it might allow increased movement of the leg and back without producing pain. Consequently, under general anesthesia, the sciatic nerve was stretched by forcible straight leg raising accompanied by strong dorsiflexion of the foot. The patient experienced an immediate decrease in pain. Two more manipulations were performed at intervals of 2 days. After the third manipulation the patient was completely relieved of discomfort, remained well, and carried on a normal, active life.

This treatment was carried out in 1948 and, during the succeeding years, the procedure has been employed in patients in whom "sciatica" remained after the operative removal of ruptured intervertebral disks, and it has been instrumental in relieving postoperative "sciatica" when the cause was the formation of adhesions about the lumbar nerve roots. If the nerve root is compressed by recurrent disk protrusion or by adjacent bone, the manipulation usually increases the pain, a phenomenon that has been helpful from a diagnostic standpoint.

The Biopsy of Breast Tumors. G. B. Sanders and D. W. Kinnaird. J. Kentucky M. A. 57:795-797 (July) 1959 [Louisville, Ky.].

As a result of mass education of the laity on the subject of breast cancer, physicians are seeing patients with tiny, nondescript breast cancers measuring often less than 1.5 cm., too small and too recent to have developed the associated signs of malignancy. These lesions are potentially curable provided prompt and proper treatment is given. Surgical biopsy is necessary for the early diagnosis of the small breast lesion. The physician must be willing to subject apparently benign, small breast nodules to surgical biopsy without reluctance, in order to pick up the early nondescript breast cancer which has not had time to develop clinical signs or features suggestive of malignancy. The reluctance of physicians to perform biopsy on breast lesions unless circumstances permit immediate radical mastectomy if cancer is found is not justifiable. No statistically significant figures are available to show that delay of 2 weeks or less between biopsy and mastectomy, both properly done, has a detectable effect on 5-year survival. Properly performed biopsy, even in an outpatient department, office, or clinic, is preferable to a "wait and see" policy, provided appropriate treatment follows the discovery of cancer in 2 weeks or less. For these reasons, it is important for surgeon and generalist alike to learn and practice a logical, skillful technique of biopsy and to be willing to employ it without hesitation, whenever indicated.

Bicipital Tenosynovitis. K. F. Spence Jr. M. Ann. District of Columbia 28:386-387 (July) 1959 [Washington, D. C.].

Bicipital tenosynovitis is one of the many lesions that have been recorded in the literature as causes of the painful, stiff shoulder. It is believed that the underlying cause of bicipital tenosynovitis is some congenital abnormality in the bicipital sulcus or groove, such as obliquity of the medial wall of the intertubercular sulcus which favors subluxation or dislocation of the tendon out of the bicipital groove. Generally, the onset is insidious, although at times it is precipitated by strenuous activity. Initially the pain is localized over the anterior and medial aspects of the shoulder. It may radiate to the body of the biceps muscle, to the flexor surface of the forearm, to the insertion of the deltoid muscle, to the inferior angle of the scapula, and even to the base of the neck. The pain may be relieved by rest and aggravated by activity at first, but later it usually becomes more or less constant. The usual physical finding is exquisite tenderness over the intertubercular sulcus and on palpation of the biceps tendon. The clinical course in young individuals is characterized by recurrent attacks of pain. The treatment of bicipital tenosynovitis is essentially conservative. The application of moist heat, rest, and restriction of motion, together with the injection of Xylocaine and hydrocortisone (directly into the tendon sheath, under the transverse humeral ligament) will relieve pain in most instances. As a rule, 3 or 4 injections at weekly intervals will produce the desired results.

Surgical intervention may be indicated when an adequate trial of conservative therapy has proved unsuccessful. The author reviewed the records of patients who had been subjected to a bicipital tendon transfer operation at the U. S. Naval Hospital, Bethesda, Md. Of the 15 patients studied 12 were male and 3 were female. The ages of these patients ranged from 19 to 53 years, with an average age of 35. All of these patients had symptoms of bicipital tenosynovitis. All had tenderness to palpation of the biceps tendon in the bicipital groove. The duration of the symptoms prior to surgery ranged from 1 month to 20 years. All of these patients had received trials of conservative therapy, with some temporary relief in a few cases. At operation some abnormality was found about the biceps tendon in all cases. This varied from chronic inflammation, adhesions, and scarring of the tissues to thickening and edema of the tendon and tendon sheath.

Eleven patients stated that their symptoms were relieved; 2 that they had attained partial relief; 1 that he had attained relief for 6 weeks, when his symptoms recurred; and 1 that the operation had not given him any relief. Only 4 patients stated that they had no pain; 8 said they had mild, intermittent discomfort, but usually of a type different from that experienced prior to surgery; 2 stated that they had moderate pain; and 1 had severe, intermittent pain. The follow-up on these patients ranged from 6 years to 3 months. They were asked if they were satisfied with the results of the operation. Eleven stated that they were completely satisfied with their results. Four of the patients were not completely satisfied. The author feels that there is a place for operative treatment in the therapy of bicipital tenosynovitis. Best results will probably be obtained if surgery is reserved for the patient with severe symptoms who has had an adequate trial of conservative therapy.

NEUROLOGY & PSYCHIATRY

Schilder's Disease with Melanoderma. B. W. Lichtenstein and P. R. Rosenbluth. J. Neuropath. & Exper. Neurol. 18:384-396 (July) 1959 [New York].

The authors present 3 boys, aged 5, 7, and 9 years, all of whom presented the clinical complex of Schilder's disease with melanoderma. In 2 of the boys only clinical studies were made, but in the third boy, who died, pathological studies were made as well. Pathologically the disease was characterized by lesions in the basal ganglions, brain stem, and cerebellum as well as in the centrum semiovale. The primary pathological process was characterized by the presence of globoid cells containing periodic acid–Schiff (PAS)–positive substance. Other primary lesions were rich in microglial rod cells. It is probable that the increase of cerebroside is related to the PAS-positive substance observed in the globoid cells. The secondary zone surrounding the primary pathological process in the centrum semiovale revealed a marked inflammatory reaction characterized by the perivascular infiltrations of lymphocytes, plasma cells, and mononuclear elements. Such inflammatory reactions are frequently observed in the acute lesions of multiple sclerosis, and probably indicate a reaction on the part of the mesodermal elements to an irritant. The gitter cells in this secondary inflammatory zone contained oil-red-O-positive material, which possibly indicates its origin from the disintegration of "normal" myelin or the conversion of PAS-positive material into neutral fat. It is of significance that, where the inflammatory reaction invaded the juxtacortical medullary substance, the "U" fibers were not spared. The involvement of the basal ganglions, pons, medulla oblongata, and cerebellum was striking, and many neuropathologists are unwilling to use the designation of Schilder's disease for such a widespread process.

The terms Schilder's disease and diffuse sclerosis have been used to designate a disorder of the brain which generally occurs in children. It is characterized clinically by muscle hypertonicity, spastic paralysis, tonic and epileptic seizures, choreoathetoid movements, cortical type of blindness, and mental deterioration. The onset is usually slow, the course is variable, but always progressive leading to a fatal termination. The disorder is characterized pathologically by diffuse and symmetrical degeneration of the white substance of the brain. Since the latter is generally associated with proliferative changes on the part of the astroglia, the term diffuse sclerosis has become popular. Schilder used the term encephalitis periaxialis diffusa, but since, in many instances, there is no evidence of inflammation and the degenerative changes involve the axis cylinders as well as the myelin sheaths, his term appears to be inappropriate. The term diffuse leuko-encephalopathy has been used and is basically correct, but there are so many conditions in which the cerebral white matter is pathological that a more specific designation is needed. Cases have been classified according to the period of onset, as the infantile, the juvenile, and the late type; according to the clinical course, as the acute, the subacute, and the chronic form; and according to the names of investigators in this field, as the Krabbe, the van Bogaert-Scholz, and the Pelizaeus-Merzbacher type. Both familial and nonfamilial forms have been described, and neither attempts at simplification nor attempts at differentiation have proved very successful. The problem of nomenclature is so complex that the authors prefer the term Schilder's disease because of its wide recognition and easy differentiation from other well-known diseases of the nervous system.

Because of the addisonian pigmentation of the skin, a careful search was made to locate the adrenal glands, but none could be found at autopsy. The authors feel that the absence of the adrenal glands lends support to the view that the melanoderma was similar to that observed in Addison's disease. The possible role of the adrenal glands in myelin metabolism is suggested by the unusual coincidence of Schilder's disease and melanoderma.

Some Viral Central Nervous System Diseases. Laboratory Studies with Emphasis on Aseptic Meningitis. N. Khoobyarian, J. Draper, A. C. Dwyer, Y. K. S. Murthy and D. N. Walcher, A. M. A. J. Dis. Child. 98:15-23 (July) 1959 [Chicago].

In a series of 245 cases of diseases of the central nervous system studied at the James Whitcomb Riley Hospital for Children during 1956 and 1957, an attempt was made to recover viral agents from the patients' stools, spinal fluid, and blood samples. The patients were classified into 4 groups according to the clinical diagnosis. There were 100 cases of poliomyelitis, 52 of aseptic meningitis, 77 of encephalitis, and 16 of miscellaneous illnesses. The group with aseptic meningitis was studied in a particularly detailed manner, and the corresponding findings constitute the main subject of this report.

A variety of pathogenic agents was recovered from 21 patients (40.4%) in the group with asceptic meningitis. Sixteen of these agents belonged to the Coxsackie viruses; the other five were ECHO virus types. Regarding the 31 patients who did not yield viral agents, an attempt was made to demonstrate the development of specific neutralizing antibodies for the strains which had been isolated. Only 2 of these 31 patients responded with an increase in neutralizing antibodies in both acute and convalescing serums. All the others possessed either a high level of antibodies to one or more strains or negligible titers in both serums. The correlation observed between the presence of viruses in the clinical specimens and a rise in antibodies in 21 patients suffering from aseptic meningitis, together with the failure to establish any other estiological diagnosis, suggests that the central nervous system disease in these cases was due to the agents which had been isolated. At the same time the negative findings in the remaining 31 patients indicate that the latter might have been infected by different types of enteric viruses.

Poliomyelitis viruses were found in stools from 78 paralytic and 11 nonparalytic patients. Only one patient in the group with encephalitis and 4 in the group with miscellaneous diseases excreted cytopathogenic agents, and these could not be identified. Comparing the clinical diagnoses with the laboratory findings there was a diagnostic error in 11% of the cases of poliomyelitis and in 17% of the cases of aseptic meningitis.

Dysmyelinogenic Leukodystrophy: Report of a Case of a New, Presumably Familial Type of Leukodystrophy with Megalobarencephaly. F. J. Wohlwill, J. Bernstein and P. I. Yakovlev. J. Neuropath. & Exper. Neurol. 18:359-383 (July) 1959 [New York].

The case presented concerned a male child who had a "large head." He did not sit up or begin to crawl until he was 18 months old. He did not walk, even with assistance, until he was 2 years old, and was never toilet-trained. He was mentally retarded, had some weakness in the right arm, and Babinski's sign was present in the right foot. The head circumference was 52 cm. The x-ray film of the skull revealed an abnormally large cranial vault contrasting with normal proportions of the facial skeleton. He died at the age of 2 years and 9 months. The family history of this child is of interest in that he was the ninth child in a series of 9 siblings. One brother aged 16 years and 3 sisters aged 11, 7, and 6 years, respectively, were said to be well; 1 sister and 3 brothers (including the child discussed) all were said to have "large heads," were called "hydrocephalic," and all died in childhood.

Autopsy was performed on the child presented, and the histopathology of the brain and spinal cord is described in detail. The outstanding features were (1) the loss of myelin sheaths in the white matter of the brain and spinal cord, especially in those areas which myelinate relatively late such as the centrum semiovale in the cerebral hemispheres and the ventral columns in the spinal cord; (2) the remarkable preservation of axis cylinders in all areas of white matter, even those totally devoid of myelin; (3) the lack of either histological or histochemical evidence for the presence of the lipoid products of myelin breakdown, but, instead, (4) the ubiquitous infiltration of the ground substance of the entire neuraxis with large amounts of almost wholly extracellular, strongly Dietrich-Smith–positive, nonbirefringent, strongly periodic acid–Schiff (PAS)–positive, probably protein-bound, water-soluble glycolipid and hydrophilic material; (5) a remarkable tolerance and inertia of the macroglial, vascular, and microglial apparatus of the brain to the presence of particles of the material which filled the ground substance like dust in colloidal suspension; (6) inspissation and massive banking of this material around the blood vessels and under the pial coverings of the neuraxis upon the parenchymal facing of the mesodermal barrier between the brain substance and the blood stream; (7) a true megalobarencephaly, without hydrocephalus or edema to account for a relative increase in size and the inordinate increase in weight of the brain; (8) the occurrence of a single transverse patch of demyelination with 2 symmetrical, frankly myeloclastic foci in the medulla oblongata; and, finally, (9) the familial character of the disease.

The authors point out that in the past 8 years, 4 children with this peculiar degenerative disease process in the central nervous system have been reported in the English and American literature. In these 4 cases the affected child was either the only child or the sibship was limited in number, so that in these 4 cases the Mendelian factor, if present, would not have been so evident as it was in the case presented here, in which 4 of a sibship of 9 children had "large heads" and died in infancy. The authors feel that on the basis of the evidence obtained in the child presented and of the 4 cases reported in the literature, the disease is a distinct and unique entity in the broad group of diffuse infantile leukoencephalomyelopathies within a still broader group of "cerebral palsies." Its relation to a certain type of diffuse degenerative diseases of childhood and its distinct position in the group of leukodystrophies can be stated best in the framework of Hallervorden's classification. The disease process represents a unique and now clearly definable entity for which the designation of dysmyelinogenic leukodystrophy is descriptive and appropriate. Such designation stresses the cardinal feature of the disease, the failure of the maturation of myelin, and of the formation of the normal myelin sheaths. The disease process is distinct from the degenerative leukodystrophies of myelinoclastic type.

GYNECOLOGY & OBSTETRICS

Endocrine Treatment of Metastasizing Mammary Carcinoma. T. Hornykiewytsch. Strahlentherapie 109:5-27 (no. 1) 1959 (In German) [Munich, Germany].

This paper presents observations on 260 patients who received treatment for metastasizing mammary carcinoma. Sixty of these patients, who were treated between 1936 and 1946, received only symptomatic treatment (group 1). Roentgen-ray castration was employed in 53 preclimacteric patients during the years from 1949 to 1951, and beginning with 1950 this treatment was given to all women under 60 years of age (group 2). Between 1951 and 1954 testosterone propionate was given to 90 women, and those less than 60 years of age were subjected to roentgen-ray castration prior to the hormone treatment (group 3). Finally, 57 patients, treated from 1952 to 1956, were given methylandrostenedriol (Methandriol), those under 60 again being subjected to roentgen-ray castration (group 4).

The patients of group 1, receiving only symptomatic treatment, served as controls. In this group the average survival time was 5.6 months; in group 2 it was 7.6 months; in group 3 it was 9.9 months; and in group 4 it was 7.5 months. The survival times of the patients showing objective improvement were 12.5 months, 17.2 months, and 12 months, respectively, in groups 2, 3, and 4, and in those showing only symptomatic improvement the survival times in the 3 treated groups were 7.2 months, 11.8 months, and 7 months. The prolongation of the average survival times in the 3 treated groups was significant, being twice or 3 times longer than that of the control group.

The mode of action and the value of roentgen-ray castration, oophorectomy, adrenalectomy, hormone treatment, and hypophysectomy are critically discussed on the basis of the aforementioned material and of reports in the literature. It seems probable that the therapeutic principle is a nonspecific one and is due chiefly to a radical but suitably directed and hormonally induced change in the tissues. Two stages are recommended for the treatment of metastasizing carcinoma of the breast: the first one consists of castration by irradiation and hormone treatment; if this is not enough, hypophysectomy by means of radioactive substances, such as radiogold (Au^{198}) or radioyttrium (Y^{90}), is employed as a second stage.

Changes in Diabetes Insipidus During Pregnancy and Lactation. R. L. Scheer, L. G. Raisz and C. W. Lloyd. J. Clin. Endocrinol. 19:805-811 (July) 1959 [Springfield, Ill.].

Despite the striking diuresis observed in patients with diabetes insipidus it is known that the defect in antidiuretic hormone production in many of these patients is incomplete, since antidiuretic responses can be elicited with certain stimuli such as the administration of nicotine. Moreover, variations in diuresis are observed with changes in the function of other endocrine glands, particularly the adrenal and thyroid. Little is known concerning the interrelation between diabetes insipidus and the endocrine changes in pregnancy, lactation, and the menstrual cycle. The authors describe observations on a woman who had first noted polydipsia and polyuria coincident with menarche at the age of 13 years. Without treatment she drank between 10 and 15 quarts of fluid each day. When she was 20 years old, a diagnosis of diabetes insipidus was made. Administration of posterior pituitary powder by nasal insufflation produced relief of symptoms. However, this was discontinued after 3 years because of nasal irritation, and the symptoms returned.

This woman has been under observation by these authors since 1951, when she was 26 years old. She is now 33 years of age, gravida 10, para 8. She repeatedly demonstrated an increase in the requirement for vasopressin during pregnancy, a decrease during lactation, and a less striking increase during the latter part of the menstrual cycle. Results of water deprivation tests on this patient suggested that endogenous antidiuretic hormone was released during lactation. Intravenous infusions of small doses of vasopressin had a pronounced antidiuretic effect on the third and twenty-eighth days of the menstrual cycle, a distinctly smaller effect during pregnancy, and a possibly smaller effect on the eighteenth day of the menstrual cycle.

Acute Pancreatitis at End of Pregnancy and During Delivery: 2 Cases. E. Elben. Geburtsh. u. Frauenh. 19:512-515 (June) 1959 (In German) [Stuttgart, Germany].

Although a textbook on internal medicine and an extensive statistical review on pancreatitis had called attention to the fact that a rather large percentage of women with acute pancreatitis or pancreatic necrosis are pregnant, the author feels that obstetricians may not be aware of this and may miss the diagnosis of pancreatitis in parturient women. In the first of the 2 women presented the pancreatitis was discovered only during revision of the abdomen after cesarean section at term. Cesarean delivery had been resorted to because of persistent severe pains in the upper abdomen, particularly in the umbilical region, associated with nausea and vomiting. Inspection of the abdomen, after delivery of the viable infant, revealed stones in the gallbladder, the cystic duct, and the choledochus, as well as hardening of the pancreas. Cholecystectomy was performed and the choledochus was opened in an effort to remove a stone impacted at the ampulla of Vater. When this failed the stone was pushed into the duodenum. After removal of several stones from the bile passages and after testing the patency of the choledochus the abdomen was closed. Recovery was retarded by exudative pleurisy.

In the second patient, a 20-year-old primipara, "pancreatitis resulting from closure of the choledochus by a stone" was suspected when, about 4 weeks before the expected delivery, she presented symptoms like those observed in the first patient. After the infant had been delivered by abdominal cesarean section, inspection of the abdomen revealed enlargement and hardening of the pancreas and a stone at the ampulla of Vater which, after cholecystectomy, was pushed into the duodenum. After removal of a series of small stones from the choledochus a T-drain was inserted, the abdomen was closed, and recovery resulted.

The author suggests that vomiting during pregnancy may occasionally be due to cholecystopathy and pancreatitis, and that these conditions may sometimes be mistaken for hyperemesis gravidarum. Determination of diastase concentration is important as a means of recognizing acute pancreatic disease and is a valuable aid in the diagnosis of acute abdominal conditions arising during pregnancy or labor.

Primary Heterotopic (Ectopic) Chorioepithelioma and Chorioepitheliosis. E. Nanke. Geburtsh. u. Frauenh. 19:523-531 (June) 1959 (In German) [Stuttgart, Germany].

The author describes the history of a 48-year-old woman who was subjected to supravaginal hysterectomy because of hydatidiform mole. Thorough histological examination of the molar mass and of the uterus did not reveal any sign of malignancy. The woman died 2 years later of a cerebrovascular accident. Autopsy revealed a small nodule, the size of a bean in the left lung, and a similar one in the right kidney. While both of these nodules were found to consist of *chorioepithelioma*, careful examination of the hydatidiform mole and of the uterus revealed no orthotopic foci of malignant chorioepithelioma. The presence of chorionic cells in the apoplectic area of the right occipital lobe was suspected but could not be definitely established, since only a few shadow-like atypical cell forms could be seen in the hemorrhagic area.

In view of the histological findings at autopsy and of the results of the microscopic examination of the hydatidiform mole and of the amputated uterus, the pulmonary and renal tumors cannot be regarded as metastases of a choriocarcinoma originating from the earlier hydatidiform mole. It is suggested that they arose from the transport of benign trophoblastic emboli to the lung and kidney, and that the term "chorioepitheliosis" (in analogy to endometriosis) should be applied to this type of lesion. The authors define the biological concept of chorioepitheliosis and, on the basis of the case presented, they explain the difference between heterotopic chorioepithelioma and chorioepitheliosis. They classify the case as one of deportation chorioepitheliosis.

PEDIATRICS

Relation of Isolated Recurrences of Sydenham's Chorea to Preceding Streptococcal Infections. A. Taranta. New England J. Med. 260:1204-1210 (June 11) 1959 [Boston].

It has been established that rheumatic polyarthritis and carditis occur 1 to 5 weeks after infections of the throat due to the group A streptococcus. Although the preceding infections may be asymptomatic, they are almost always detectable, in retrospect, by titration of streptococcic antibodies. On this fact the theory of the streptococcic etiology of rheumatic fever was based. This theory was confirmed by the reduction in the recurrence rate of rheumatic fever achieved through antistreptococcic prophylaxis and by the close relation of the recurrences that do occur to preceding streptococcic infections. Contrariwise, in cases of Sydenham's chorea—a disorder frequently but not constantly associated with rheumatic polyarthritis and carditis—all evidence of recent streptococcic infection is often lacking. This frequent lack of evidence of recent streptococcic infection, added to the frequent absence of laboratory signs of "rheumatic activity" in cases of chorea, lends support to the view that Sydenham's chorea is of two kinds, "rheumatic" and "nonrheumatic," differing not only in manifestations but also in etiology. An explanation of these findings was suggested by a previous study showing that when chorea, rheumatic polyarthritis, and carditis occur in the same patient, chorea tends to appear later than the other 2 manifestations.

This paper is concerned with 60 children who had had Sydenham's chorea, and were therefore susceptible to recurrences. They were followed over a 6-year period in 2 antistreptococcic prophylaxis clinics. A unique feature of these clinics was the routine periodic testing of throat cultures and streptococcic antibodies, permitting the detection and dating of even subclinical streptococcic infections with high reliability. There were no recurrences of chorea in the 41 children who did not have streptococcic infections. Of 19 patients who had one or more streptococcic infections, 3 had recurrences of chorea. The recurrences were not preceded or accompanied by rheumatic polyarthritis or carditis, and their clinical onset was 3 to 6 months after the first immunological evidence of streptococcic infection. They were not accompanied by a high erythrocyte sedimentation rate or a positive test for C-reactive protein, except in 1 patient who had a second recurrence of chorea shortly after the first recurrence and an intervening streptococcic infection. These data provide the first available evidence that Sydenham's chorea can follow infections with group A streptococci by an interval longer than rheumatic polyarthritis and carditis, even in the absence of the latter manifestations and, indeed, in the absence of "rheumatic activity."

Effect of Corticotropin in Exudative Erythema Multiforme (Stevens-Johnson Syndrome). B. Lindquist. Nord. med. 61:784-785 (May 21) 1959 (In Swedish) [Stockholm].

In a case of exudative erythema multiforme (Stevens-Johnson syndrome) in a boy aged 11, treatment with corticotropin brought prompt and marked improvement. The effect was especially striking against the background of unfavorable development of the disease during the first couple of days, when the patient was treated with only tetracycline. The good response to corticotropin or adrenal steroids in this and similar cases reported in the literature supports the view that the syndrome is due to a hyperergic reaction to a nonspecific agent.

A Genetic Profile of Infantile Amaurotic Family Idiocy. Statistical Evaluation of One Hundred Thirty-One Patients. S. M. Aronson, B. E. Aronson and B. W. Volk. A. M. A. J. Dis. Child. 98:50-71 (July) 1959 [Chicago].

Data on 131 cases of infantile amaurotic family idiocy (IAFI) were obtained through a questionnaire sent to the patients' families, including questions on the nature of birth, time and form of onset of the disease, family background, and familial and sex incidence. This report is a statistical analysis of the data thus obtained, supplemented with clinical observations made during hospitalization by the doctors cooperating in this study. A control group was formed with paired siblings of the same sex, differing from the carriers of IAFI only in not showing the disease. The only other variable introduced was Jewish parentage. Only 4 of the 102 families analyzed were non-Jewish.

No statistically significant differences were found between the IAFI group and the control group as to the nature of pregnancy, the duration and quality of labor, and the infant's weight at birth. The average duration of the disease was 24.1 months and the average age at death was 29.5 months with no apparent difference between the sexes. The condition of infants of non-Jewish extraction seemed to deteriorate more rapidly than that of Jewish infants. The age of the parents was rarely over 35 years. Less than 1% of the mothers and about 9% of the fathers were 40 years or older at the time the infant had been born.

In the 102 families studied there were 122 infants with IFAI. Subtracting 23 families who had only one child, there were multiple cases in 25% of the remaining 79. The disorder is undoubtedly of a familial nature. As 95% of the families included in this analysis had only three or fewer children, the number of cases was not sufficiently large for a statistical verification of the recessive gene-substitution mechanism in the frequency of IAFI. No significant difference in the sex incidence was observed. Taking into consideration the order of birth, the frequency of the disease in the female group was highest in the first-born and decreased as the rank order rose. In the male group the trend was in the opposite direction, the percentage of incidence of IAFI rising with the succeeding rank order.

The Prophylaxis of Streptococcal Infections in Patients with Rheumatic Fever. A Comparison Between Sulfadiazine and Erythromycin. M. T. Stahlman and F. W. Denny. A. M. A. J. Dis. Child. 98:59-71 (July) 1959 [Chicago].

Fifty children from the Vanderbilt Hospital Pediatric Cardiac Clinic were included in this comparative study of sulfadiazine and erythromycin as prophylactic agents against streptococcic infection in patients with rheumatic fever or rheumatic heart disease. Twenty-five of the children were selected at random and placed on a continuous treatment consisting of 0.5 Gm. of sulfadiazine in the morning and at night. The other 25 were given 100 mg. of erythromycin (Ilotycin) also in the morning and at night. There were 9 males and 16 females in the sulfadiazine group, with an average age of approximately 12 years; and 19 males and 6 females in the erythromycin group, with an average age of approximately 10½ years. The patients in the first group were observed for an average of 19.5 months, none for less than 7 months; those in the second group were observed for an average of 19.5 months, none for less than 9 months. All children were followed closely at 2 to 3 week intervals during the active phase of their disease, and at increasing intervals up to 3 months after their symptoms had subsided. During each clinic visit throat cultures for β-hemolytic streptococci were obtained, totaling 305 cultures from the sulfadiazine and 369 from the erythromycin group.

In the sulfadiazine group positive streptococcic cultures were obtained from 11 patients, with group A streptococci found in 7 of them. Four of these 7 patients had clinical symptoms of respiratory infection associated with the positive culture for group A streptococci. One child, who had shown no signs of rheumatic activity for four years, developed a recurrence characterized by arthritis and carditis. This was the only recurrence in the entire series of 50 children. In the erythromycin group, throat cultures from 8 patients yielded β-hemolytic streptococci, with group A isolate in only one. In this patient the positive culture was associated with a respiratory infection, but no significant rise in antistreptolysin titer was observed. Both sulfadiazine and erythromycin were well tolerated. Erythromycin was considered a superior agent for long-term preventive treatment against streptococcic infection in patients who have had rheumatic fever.

Hodgkin's Disease (Malignant Lymphogranulomatosis) During Childhood. E. Loder. Helvet. paediat. acta 14:141-183 (June) 1959 (In German) [Basel, Switzerland].

The author presents observations on children with Hodgkin's disease treated at the University Children's Clinic in Zürich. In 1929 Feer had described 9 children with Hodgkin's disease observed at the clinic, and since 1929 17 more children with this disease have been observed. While this report is concerned chiefly with the 17 children, all 26 cases are considered in the statistical analysis. Between 1947 and 1956 the annual mortality from Hodgkin's disease in Switzerland was 17 per 1 million inhabitants, and it is noteworthy that England and Wales, as well as the United States of America, report about the same mortality from Hodgkin's disease. About 15% of cases of Hodgkin's disease occur in children. Male predominance is even more pronounced in children than in adults. Of 366 pediatric cases reported in the literature, 83.6% were boys. Hodgkin's disease seems to inhibit the development of secondary sex characters; this was demonstrated in 9 of the author's patients in whom the disease existed during the period of puberty (12 to 17 years). In infants the disease is rare, but the incidence is rather high between 2 and 6 years of age.

The time of onset and the first localization may be difficult to ascertain, as swelling of the lymph nodes may often remain unrecognized for a time. Swelling of the lymph nodes in the neck was the first symptom in 24 of the 26 patients. General symptoms in the form of fever, sweats, lack of appetite, loss of weight, fatigue, and pallor were noted at the onset in 19 patients. Mediastinal lymphomas are always present late in the course, but in 15 patients of this group they were already evident during the first 4 months. The combination of cervical and mediastinal lymphadenopathy is an important diagnostic factor in Hodgkin's disease. While the symptomatology is generally about the same in children as in adults, splenomegaly is often more marked, the mediastinal localization is more frequent, and fever generally appears early in children. A tendency to pleural involvement, clinically manifest as pleural exudate, is especially pronounced in children. Lymphopenia is the most constant change in the blood picture.

Roentgen-ray irradiation is still the main therapeutic weapon together with surgical treatment in selected cases. Cytostatic drugs are helpful only as adjuvants, because, when employed alone, they only produce brief remissions. The prognosis varies in children as it does in adults. Life expectancy ranges from a few weeks to several decades. The average survival in a series of 174 children under 15 was 38 months. The ultimate prognosis is determined less by the treatment than by the nature of the disease. Why the progress of Hodgkin's disease differs from case to case is still obscure. Patients have been known to survive without any specific therapy for 25 and more years, while others died within a few months.

Thallium Poisoning. Report of Two Cases. M. D. Stein and M. A. Perlstein. A. M. A. J. Dis. Child. 98:80-85 (July) 1959 [Chicago].

Clinical manifestations of thallium poisoning are sometimes confusing and may simulate other conditions. The authors report on 2 such cases of unclear picture that they observed at the Cook County Children's Hospital; in both cases ataxia was the main clinical symptom. The first patient was a 4-year-old boy admitted to the hospital because of unsteady gait, loss of hair, tremor, and lethargy of 2 days' duration. A mild pharyngitis and urinary infection were also present. The laboratory tests were all normal. A diagnosis of acute cerebellar ataxia of unknown origin was made and the patient was given penicillin and sulfisoxazole (Gantrisin). The pharyngitis and urinary infection cleared up promptly but the ataxia and alopecia became progressively worse. The child developed hyperkeratosis of the palms and soles, which completed a clinical picture suggestive of either thallium or arsenic toxicity. An empirical therapy with dimercaprol (BAL) was started, in a daily dose of 2.5 mg. per kilogram, divided into 4 intramuscular injections. Three days later the child was much worse. The dose of dimercaprol was increased to 5 mg. per kilogram a day, and trihexypenidyl (Artane) was added to the treatment in a dose of 2.5 mg. per kilogram three times a day. The results were immediate and dramatic. The child was discharged as clinically cured, after a 7-week hospitalization.

The second patient was a 3-year-old boy suffering from cerebral palsy due to kernicterus, who had been followed up at the outpatient department. After an absence of 6 months from the clinic the patient returned because of an unsteady gait which had become gradually worse during the previous 4 months. He also had parietal alopecia. The diagnosis of thallium poisoning was made and later confirmed by laboratory tests. The patient did not keep his next appointment at the clinic; it was reported later that his ataxia and alopecia had disappeared spontaneously. Seven months later the child was brought back and hospitalized because he had stopped walking since the day before. On admission there was no alopecia, but the child was irritable and refused even to stand up. Two days later he began to walk with an ataxic gait; marked tremor was observed, and 8 days after admission a patchy alopecia appeared. A combined therapy was instituted with daily administration of 5 mg. per kilogram of dimercaprol divided into 4 intramuscular doses, and 2.5 mg. per kilogram of trihexyphenidyl 3 times a day. The child was discharged in good condition after 6 days of this combined therapy. In both cases moderate doses of dimercaprol appeared to be effective in achieving detoxification while trihexyphenidyl was effective in relieving the tremor.

THERAPEUTICS

Report on a Survey of Allergic Reaction to Penicillin. Investigation Conducted by the Research Committee of the Australian College of General Practitioners. Recorder, N. A. Andersen. M. J. Australia 1:827-830 (June 20) 1959 [Sydney].

In a survey conducted by the Research Committee of the N. S. W. Faculty of the Australian College of General Practitioners, data on 6,832 patients who had received systemic treatment with penicillin were compiled. This series comprised 2,874 men, 2,432 women, and 1,526 subjects whose sex had not been stated. Reactions to penicillin occurred in 88 (1.3%) of the patients; 60 of these were men, 27 were women, and in one case the sex had not been declared. These figures show a male:female ratio of 2:1 which is statistically significant. The reactions were classified into immediate, when occurring within 30 minutes of the administration of penicillin, and delayed, when occurring hours or days later. Immediate reactions occurred in 7 patients. Six of them had received penicillin previously, and 3 had sustained a previous reaction. Five patients in this group had received procaine penicillin, one crystalline, and one benzathine penicillin. Procaine penicillin had been given to 63 of the 74 patients in the delayed reaction group, benzathine penicillin to 6, and crystalline penicillin to 4. Other types administered included combined forms and oral penicillin. In 2 cases the specific type used was not known. There was a record of allergic background in 47 of the delayed reaction cases; in 14 there was no information concerning previous allergic manifestations.

Taking the series as a whole, procaine penicillin had been given to 4,763 patients, with reaction in 68 (1.4%); benzathine penicillin to 159, with reactions in 6 (3.8%); crystalline penicillin to 287, with reactions in 5 (1.7%); combined penicillin injections to 344, with reactions in 7 (2%); and oral penicillin to 566, with reactions in 3 (0.5%). In 796 cases in which there were 2 reactions, the type of penicillin was not known. A comparison of these percentages indicates that there is a somewhat greater risk of provoking a reaction when a benzathine penicillin is used. As the figures supporting this suggestion are very small, additional inquiries are needed in this respect. It should be noted that of the 10 patients showing reaction to benzathine penicillin, 3 suffered a recurrence of the symptoms. The report emphasizes the importance of a preliminary assessment of the likelihood of a patient's developing an anaphylactic reaction. Administration of testing doses per skin scratch and the conjunctival sac technique is recommended.

The Value of Anticoagulant Therapy in the Treatment of Acute Myocardial Infarction. J. A. W. McCluskie and D. A. Seaton. Scottish M. J. 4:305-309 (June) 1959 [Glasgow].

In order to clarify the conflicting views on the use of anticoagulants in the treatment of myocardial infarction, a study was carried out over a 5-year period (1952 to 1956) on a total of 226 patients with myocardial infarction. All the patients had recent (24 hours) myocardial infarction, and not one was included in this series who had a history of previous myocardial infarction, peptic ulcer, liver disease, or severe renal disease. The electrocardiograms in all patients showed a pathological Q wave. The patients were divided into 2 groups, the first consisting of 115 patients who were given anticoagulants, and the second of 111 patients who were not given anticoagulant treatment. The anticoagulant drugs used were heparin and ethyl biscoumacetate (Tromexan) until early 1954, and thereafter heparin and phenindione (Dindevan). Heparin was given only in the first 48 hours.

In the first group 21 (19%) patients died, and in the second group 45 (39%) patients died. In the second group of patients who did not receive anticoagulant therapy 33% of the males and 65% of the females died, as compared to 16% and 27%, respectively, in those receiving anticoagulant therapy. The mortality as a whole and for each sex in the group receiving anticoagulants was about half of that of the treated group. Thromboembolic episodes occurred in 39 (39%) of the untreated group and in only 20 (18%) of the treated group. The results obtained in this series indicate a marked improvement in the outlook of the patient admitted to the hospital with a first attack of myocardial infarction, provided he survives the first 24 hours, and justify the routine use of anticoagulant therapy in all patients with myocardial infarction.

V. Willebrand's Disease and Its Treatment with a Specific Plasma Fraction. J. E. Jorpes. Scottish M. J. 4:269-275 (June) 1959 [Glasglow].

A review of the literature on Von Willebrand's disease (hereditary pseudohemophilia) up to 1956 showed that no agreement could be reached as to whether the underlying deficiency in this disease is a qualitative platelet insufficiency or a vascular disorder, or both, or whether the deficiency might vary from patient to patient. Since 1956, I. M. Nilsson and co-workers in Sweden have studied 20 patients (11 females and 9 males) with severe hemorrhagic diathesis characterized by deficiency of antihemophilic globulin (between 1 and 10% of normal), a prolonged bleeding time, a normal platelet count, and platelets which behaved normally in the thromboplastin generation test. Plasma human fraction I-O of Blombäck and Blombäck containing antihemophilic globulin A has been administered intravenously on 45 occasions in 9 of these patients in connection with hysterectomy, tooth extractions, intra-abdominal bleeding, large hematomas, epistaxis, and other bleeding episodes. The bleedings were controlled by this fraction, and the prolonged bleeding time was corrected in all of these 9 patients, even if antihemophilic globulin, factor VIII activity, was lacking. The authors believe that the prolonged bleeding time in patients with v. Willebrand's disease is attributable to a deficiency in a plasma factor other than fibrinogen and the antihemophilic globulin, and not to the abnormalities of the capillary walls. Quantitative determinations of the antihemophilic globulin content of the plasma in the families of the patients have shown that one of the parents and several members in each family exhibited a lower than normal antihemophilic globulin level of the plasma without any pronounced bleeding symptoms.

In view of the clinical and genetic similarity between this hemorrhagic diathesis and that of v. Willebrand's pseudohemophilia, the authors studied 16 patients in whom v. Willebrand had made his original observations. All the patients had a decreased antihemophilic globulin level of plasma between 30 and 60% of normal. In all the patients platelets were normal with regard to count and behavior in the thromboplastin generation test. The prolonged bleeding time in one of v. Willebrand's patients could also be corrected with the I-O plasma fraction of Blombäck and Blombäck. Both conditions have been shown to be transmitted as an autonomal dominant gene with varying expressivity. The two hemorrhagic diseases, consequently, seem to be closely related, if not one and the same disease.

PATHOLOGY

Co-existent Tuberculosis and Carcinoma of the Lung. G. H. B. Baker. Ulster M. J. 28:69-71 (May) 1959 [Belfast, Ireland].

While it has been suggested that pulmonary tuberculosis and bronchial carcinoma are antagonistic, it has also been asserted that tuberculosis is an etiological factor in carcinoma. When the author noted both conditions in the course of a routine postmortem study, he decided to study the records of the department of pathology of Queens University, Belfast, in an attempt to assess the significance of the co-existence of these diseases. In 13,000 autopsies recorded between 1937 and July, 1958, a total of 357 cases of bronchial carcinoma were found, which in 12 cases was associated with active pulmonary tuberculosis. The tuberculous and carcinomatous lesions were on the same side of the lung in 10 of the patients, on different sides in 1, and in 1 the location of the carcinoma was not recorded. The incidence of active tuberculosis in cases with carcinoma was not statistically different from cases without carcinoma. It seems likely that carcinoma may occasionally arise in a lung already the site of a tuberculous cavity. It is suggested that the existence of a bronchial carcinoma may increase the fulminance of a tuberculous lesion in the affected lung. The co-existence of the two conditions is becoming more common, both because of the increased incidence of bronchial carcinoma and because of the fact that tuberculosis is now occurring in the older age groups.

Bronchiolar (Peripheral Lung) Neoplasms and Previously Undescribed Observations on the Origin of Bronchiolar Carcinoma. S. L. Eversole Jr. and W. F. Rienhoff. J. Thoracic Surg. 37:750-765 (June) 1959 [St. Louis].

The authors report on 4 patients, between the ages of 58 and 76 years, who died in the Johns Hopkins University Hospital and on whom routine autopsies were performed, which revealed definitely benign adenomatous tumors or malformations of the bronchioles. These lesions were well circumscribed but not encapsulated single nodules lying beneath the pleura in the peripheral lung fields and were composed of thick fibrous septums covered by a layer of benign-appearing cuboidal, non-mucus-forming, nonciliated epithelium. In 2 of these 4 patients these tumors were larger and the centers were hyalinized. The thickened fibrous septums at the margins merged imperceptibly with the alveolar septums and, in appropriate stains, the thickened septums and hyalinized cores were seen to contain large numbers of elastic tissue fibers. The smaller of these lesions thus strongly suggested that they were malformations, and the larger ones had characteristics of frank tumor at their periphery, but retained the malformation-like structure centrally.

The cases of 2 additional patients, aged 69 and 53 years, are reported, who were successfully operated on for slowly growing localized bronchiolar carcinomas. Microscopic examination of the surgical specimens showed striking similarity to the incidental autopsy findings in the previous 4 patients. In the surgical specimens, however, the epithelium outside the hyalinized areas was more luxuriant and exactly reproduced the histological picture of the non-mucus-forming type of bronchiolar carcinoma. The new concept that bronchiolar carcinoma may arise from bronchiolar adenomatous malformations, in single or multiple foci, is put forth.

An additional case is reported of a 68-year-old woman who died of congestive heart failure, and in whom a single small nodule of pulmonary adenomatosis was found on autopsy. Histologically, this tumor nodule showed tall columnar mucus-producing epithelium which formed a one-cell-layer-membrane lining of alveolar septums. The nuclei lay at the base of the cells. The alveolar septums were not thickened or appreciably scarred. The case of this patient has been included only to contrast its histological picture with that of the bronchial tumors in the other 6 patients. While in the literature, for the most part, pulmonary adenomatosis and its malignant counterpart, alveolar cell carcinoma, are indiscriminately grouped with bronchiolar carcinoma, these 2 diseases, in the authors' opinion, are different in nature and should not be grouped together.

Experimental Investigations of Lipid Metabolism in Ischemic Myocardium. M. Ursini, V. Pastore and A. Ciardiello. Minerva chir. 14:417-426 (April 30) 1959 (In Italian) [Turin, Italy].

Changes of the serum total lipid, phospholipid, and cholesterol levels in experimentally produced ischemic myocardium were studied in 30 dogs. The anterior descending branch of the left coronary artery was ligated at about 10 to 15 mm. from its origin. This procedure produced infarcts in a predictable location. Blood samples were obtained simultaneously from the coronary veins, right atrium, and femoral artery. The blood samples were collected at intervals from 1 hour to 45 days after ligation. At most 2 specimens were obtained from each dog. Total serum lipid values decreased slightly during the first several hours after ligation and then began to increase reaching the peak recording 24 hours after ligation. Subsequently serum total lipid values decreased; they were restored within the normal limits 10 days after ligation and stabilized at subnormal levels during the period from 25 to 45 days after the induced infarction.

Serum phospholipid values increased in all 3 locations of the circulation after the infarction. Changes were slight and transitory in the venous atrial blood and in the systemic arterial blood, reaching the maximum values 24 hours after the infarction. The values were restored to normal levels 15 days after the infarction. Total serum phospholipid values increased more markedly and lasted longer in the blood obtained from the coronary veins. Its peak values were observed 24 hours after the infarction and remained at higher than normal values even at the end of the investigation. Serum cholesterol levels first increased, reaching peak values 12 hours after the infarction. The values were restored within the normal limits within 15 days and then increased slightly and stabilized between 25 and 45 days after the infarction. This study reveals that lipid metabolism changed considerably after development of the ischemic myocardium. The changes were probably related both to produced lesion of the myocardium and to the decrease of the oxygen flow into the myocardium.

Penicillin-Resistant Staphylococci: Incidence in Outpatients with Hand Infections. A. J. Buhr and J. C. Scott. Lancet 1:1019-1021 (May 16) 1959 [London].

To obtain an indication on the incidence of penicillin-resistant strains of Staphylococcus aureus among members of the general population for the Oxford area, the authors studied strains isolated from hospital outpatients from the Oxford accident service who presented hand infections. These were chosen because in 1952 it had been noted in this unit that of 82 Staph. aureus hand infections in which penicillin resistance was tested, no resistant strain was found. In 1957 Staph. aureus was obtained from 294 outpatients with hand infections, of whom 23 were doctors, nurses, physiotherapists, or wardmaids. There were therefore 267 members of the "general public" from whom 271 swabs were taken; of these 81 grew penicillin-resistant strains of Staph. aureus. Eighty of these penicillin-resistant strains were also tested for sensitivity to chlortetracycline; 5 of these were found to be resistant. Of the 23 hospital staphylococcus contacts from whom 25 swabs were cultured, 17 grew penicillin-resistant staphylococci; 5 of these organisms were resistant also to chlortetracycline. Of the 271 swabs, 187 were obtained from patients who had not been treated with penicillin, while the remaining 84 swabs were obtained from patients who had had penicillin therapy. Of the 187 specimens, 50 grew penicillin-resistant strains of Staph. aureus as compared to 31 of the 84 specimens obtained from patients who had received penicillin. In order to provide a larger series of hospital contacts for comparison, the authors summarized the results of a separate review of all proved Staph. aureus hand infections in nurses treated as outpatients in the accident service between January, 1954, and April, 1958. In this group, 51 of 58 strains of staphylococci were found to be resistant to penicillin. A further analysis of these findings showed that from January, 1956, until April, 1958, 30 out of 31 nurses with Staph. aureus hand infections had a penicillin-resistant staphylococcus. With "hospital staphylcocci" so often resistant to penicillin, all available methods should be used to reduce hospital infections. The introduction of antibiotics has increased the importance of all forms of aseptic and antiseptic precautions.

BOOK REVIEWS

Diseases of Metabolism: Detailed Methods of Diagnosis and Treatment. Edited by Garfield G. Duncan, M.D., Professor of Medicine, University of Pennsylvania, Philadelphia. With contributions by Walter Bauer and others. Fourth edition. Cloth. $18.50. Pp. 1104, with illustrations. W. B. Saunders Company, 218 W. Washington Sq., Philadelphia 5; 7 Grape St., Shaftesbury Ave., London, W. C. 2, England, 1959.

Few fields of medicine are changing with the rapidity that has characterized the general area of metabolism. This new edition represents a welcome improvement of a book that has been valuable since 1942. The format is similar to that of the previous editions. Introductory sections on carbohydrate, protein, and lipid metabolism are well written. There is also a chapter on mineral metabolism and a new chapter on water balance in health and disease. The vitamins, avitaminosis, undernutrition, and obesity are discussed. All the chapters represent authoritative reviews and include discussions of such relatively new concepts as the role of nonesterified fatty acids. The section on diabetes and hypoglycemia represents a practical guide to the treatment of these disorders, including discussion of the various insulins and a brief discussion of tolbutamide. Juvenile diabetes is also discussed. As in the past, this book remains the standard guide of the physician and specialist who needs help in understanding metabolic problems. A list of references follows most of the chapters, including some 860 references for the chapter on diseases of the thyroid. A useful appendix includes height, weight, and growth curves.

DDT: The Insecticide Dichlorodiphenyltrichloroethane and Its Significance. Edited by Paul Müller. Volume II: Human and Veterinary Medicine. Edited by S. W. Simmons. Authors: W. J. Hayes, Jr., S. W. Simmons, and E. F. Knipling. Chemische Reihe, Band 10, Lehrbücher und Monographien aus dem Gebiete der exakten Wissenschaften. Cloth. 66 Swiss francs; 66 marks. Pp. 570, with illustrations. Birkhäuser Verlag Basel, Basel, Switzerland, 1959.

This second of a three-volume series on DDT is devoted to the significance of the insecticide in human and veterinary medicine. It presents an exhaustive array of material on the pharmacology and toxicology of DDT and its medical contribution through the control of insect vectors. Part 1 of this volume is devoted to a detailed review of the basic pharmacology of DDT, its toxicity for man on the basis of experimental exposure and use, and the practical problems involved in the hazards of DDT to man and useful animals.

Part 2 contains chapters discussing the hygienic, economic, and social benefits of DDT to mankind. The problem of the resistance to DDT among arthropods of public health importance, types and mechanisms of resistance, and the significance and future outlook of resistance are considered in this section. The author stresses that, irrespective of the resistance problem, DDT and other chlorinated hydrocarbon insecticides, which were developed as a result of the discovery of DDT, are still the principal weapons in the global fight against malaria, typhus, and other arthropod-borne diseases. It is doubtful that any class of substances other than antibiotics has been found which protects more people against more diseases over a larger area than DDT. Irrespective of future developments, the discovery of DDT will always remain a historic event in the fields of public health and agriculture.

The value of DDT in veterinary medicine is discussed in part 3. The importance of DDT in the control of arthropods which attack man and its use in the veterinary field were by-products of World War II investigations. Intensive research and field efforts have been conducted in many parts of the world to determine the maximum efficiency, safety, and economy of DDT for controlling external parasites of livestock, poultry, and pets. This volume was prepared by three prominent government scientists closely identified with the study and application of this insecticide in the control of insect vectors of disease. It presents a detailed and well-balanced account of the subject which is of value to persons concerned with public health and problems of application of chlorinated hydrocarbon insecticides but should also interest a wide circle of research workers in medicine, industry, and science.

Colorimetric Determination of Traces of Metals. By E. B. Sandell, Ph.D., Professor of Analytical Chemistry, University of Minnesota, Minneapolis. Chemical Analysis, volume III. Series of monographs on analytical chemistry and its application. Editors: Beverly L. Clarke, P. J. Elving and I. M. Kolthoff. Third edition. Cloth. $24. Pp. 1032, with 110 illustrations. Interscience Publishers, Inc., 250 Fifth Ave., New York 1; Interscience Publisher, Ltd., 88-90 Chancery Lane, London, W. C. 2, England, 1959.

This new edition of an excellent work on the microanalysis of metals is about 50% larger than the second edition which appeared nine years ago. The text has been expanded about equally throughout, which indicates an increased application of microanalysis of metals as well as an increase in the available techniques of separation and colorimetric determination. The first four chapters are

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devoted to the theory of colorimetric trace metal analysis; the separation techniques such as precipitation, chromatography, and extraction; colored complex formations; and color determination. The remainder of the book is divided into chapters which cover the analysis of individual metals. The available methods of metal analysis are discussed and the preferred methods are presented in detail. The applications of these methods are dealt with in a discussion of the modifications necessary for separation and isolation from different mediums. Of interest to the investigator in medical fields are the sections that deal with the determination of trace metals in "bio-materials."

The text covers the published methods through 1957. The literature of 1958 is covered by references in addenda to each chapter. This work is not, however, a mere survey of the literature of metal microanalysis, nor a collection of methods scattered in the literature, but rather a well-written and complete textbook in which each of the methods presented is critically examined and evaluated. For the working analyst the details of the preferred procedures and the author's comments thereon are presented in a practical manner; special precautions are indicated in footnotes. There is comment on the less satisfactory methods, and any valuable observations derived from them are related to the preferred methods. The users of previous editions of this book should welcome the addition of more recent methods and techniques as well as the valuable comment and criticism of the author. It should prove a valuable addition to the library of any investigator interested in the analysis of trace metals.

Worth and Chavasse's Squint: The Binocular Reflexes and the Treatment of Strabismus. By T. Keith Lyle, C.B.E., M.A., M.D., Surgeon (and Medical Officer in charge of Orthoptic Department), High Holborn Branch of Moorfields Eye Hospital, London, and G. J. O. Bridgeman, M.C., M.A., M.B., Surgeon (and Medical Officer in charge of Orthoptic Department), Western Ophthalmic Hospital (St. Mary's Hospital), London. Ninth edition. Cloth. $10. Pp. 392, with 214 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Baillière, Tindall & Cox, 7 & 8 Henrietta St., London, W. C. 2, England, 1959.

This book is a revision and reorganization of the material which appeared in the eighth edition. It is unfortunate that the only trace of Bernard Chavasse's brilliant literary style is to be found in the quotations which head each chapter, but it must be admitted that the reorganization of the book is for the better. The book now stands as a clear-cut exposition of Chavasse's ideas with regard to the cause and pathogenesis of strabismus. The authors naturally have added their own ideas, but without obscuring Chavasse's principal thesis. The last chapter, entitled Incidence of Squint and Theories of Causation, is particularly interesting in that it presents a concise review of and critical comment on past theories on the cause of squint. No mention is made of the two aspects of strabismus that are currently prominent—the accommodation convergence to accommodation ratio and the A and V syndrome.

This book has a pleasing format and excellent illustrations. It is highly recommended to anyone interested in the heterotropias. In its present form it should be especially useful to the neophyte.

Physiotherapy in Obstetrics and Gynaecology (Including Education for Childbirth). By Helen Heardman. Revised by Maria Ebner, M.C.S.P., Principal of School and Department of Physiotherapy of United Leeds Hospitals, Leeds. With forewords by W. C. W. Nixon, M.D., F.R.C.S., F.R.C.O.G., Professor of Obstetrics, University of London, London, and Veronica Shand, S.R.N., S.C.M., M.T.D., Supervisor of Midwives, Lancashire County Council, England. Second edition. Cloth. $5. Pp. 244, with 97 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

As this edition was nearing completion its author met an untimely and tragic death in an automobile accident while she was on her way to one of her patients. This made it necessary for one of her colleagues, who refers to herself as "a member of the large community of physiotherapists who are continuing her work [Mrs. Heardman's] for the benefit of the expectant mother," to revise and complete the edition. The original author prepared this work as a "comprehensive book on physiotherapy in the fields of obstetrics and gynaecology." The writer of the foreword comments that anyone reading the book "will appreciate the contribution Mrs. Heardman made to the alleviation of unnecessary suffering, particularly in childbirth."

The book is divided into three parts entitled (1) Female Reproductive Function, (2) Physiotherapy in Obstetrics (Including Education for Childbirth), and (3) Physiotherapy in Gynaecology. Like Grantly Dick-Read's book on "Natural Childbirth," this volume provides a description of prenatal exercises to prepare the mother for childbirth but, in addition, it covers many other phases of physical therapy as related to obstetrics and gynecology. Sections on various phases of preparation for labor discuss (1) methods of arranging instruction, (2) physical instruction, (3) mental instruction, and (4) rehearsal of labor. There is also a section on preparation for lactation and education for breast feeding, and a section on postnatal restoration. In the section on physiotherapy in gynecology various physical therapeutic measures for the management of disorders of the menstrual cycle are described, and the use of physical therapeutic measures in the management of gynecologic operations and postoperative complications is discussed. Many physicians may question some of the procedures recommended in the chapter on electrotherapy in gynecology, such as "ionisation of the cervix for chronic endocervicitis"; the use of "intrapelvic faradism" for "lax pelvic floor," or faradism for "sagging breasts due primarily to muscular weakness."

Nevertheless, there are certain portions of this book that should be helpful in guiding the physical therapist in providing suitable exercises, both prenatally and postnatally. This book, written primarily for the physical therapist as a guide in a special phase of physical therapy, should also be of interest to obstetricians, gynecologists, and physicians specializing in physical medicine and rehabilitation.

The writer of the foreword, a collaborator of Mrs. Heardman's, concludes: "I have for many years appreciated the part that physiotherapy has played in rehabilitation after operations and confinements. But, with the passing of these years, I now realize that the contribution that physiotherapy can make is just as great in preventative as in curative medicine."

Surgery of the Foot. By Henri L. DuVries, M.D., Clinical Instructor in Surgery, Chicago Medical School, Chicago. Foreword by Karl A. Meyer, M.D. Introduction by Edward L. Compere, M.D. Cloth. $12.50. Pp. 494, with 403 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

The text of this new and stimulating volume brings into focus, very thoroughly, the latest as well as the formerly well-established operative procedures on the foot. It leaves the field of palliative pads, supports, shoes, and minor surgery of foot care usually included in textbooks on treatment of the foot, to present a precise and clear treatise covering all the well-established diagnostic and operative information necessary as a teaching reference as well as for guidance of the physician and surgeon who finds himself responsible for relief of foot problems requiring operation. The book is well illustrated, and the subject matter is well supported by a bibliography which indicates careful research. The author is to be congratulated on the accomplishment of this worthy endeavor.

Insecticide Resistance in Arthropods. By A. W. A. Brown, Ph.D. *World Health Organization monograph series no. 38.* Cloth. 25 shillings; $5; 15 Swiss francs. Pp. 240, with illustrations. World Health Organization, Palais des nations, Geneva, Switzerland; Columbia University Press, International Documents Service, 2960 Broadway, New York 27, 1958.

This monograph was written with the aim of covering all that is known to date on insecticide resistance in those arthropods that affect man and animals, including unpublished material communicated to the World Health Organization Expert Committee on Insecticides in the past decade. The word "resistance" applies when insecticide dosages that were formerly effective meet with control failure. In view of its importance to public health, it is not surprising to find so extensive a literature on this subject. The monograph is divided into four chapters devoted to the nature and characterization of insecticide resistance, the groups of insects that characteristically are or are not vectors to man, the development of resistance all over the world, and the physiology of resistance to DDT and other insecticides. It is concisely and clearly written, and its practical value is increased by numerous tables and detailed charts that consider increase of resistance, progress of eradication campaigns, and susceptibility of DDT and other insecticides to the development of resistance and show the location of places mentioned in the text.

The difficulty of distinguishing between natural behavioristic resistance and that developed under insecticide treatment has been a source of confusion. Foreknowledge of when resistance will start and how far it will spread will be a great step toward safeguarding the invaluable advances in health already achieved by control campaigns. This book should be valuable as a reference source to available information on the public health problem of disease vector resistance to insecticides.

What Next, Doctor Peck? By Joseph H. Peck, M.D. Half cloth. $3.50. Pp. 209, with illustrations. Prentice-Hall, Inc., Englewood Cliffs, N. J.; 70 Fifth Ave., New York 11, 1959.

This is the narrative of a young physician who got his start with a railroad construction gang in Utah. It is written in popular style with a minimum of technical detail and a liberal sprinkling of humor —much of it earthy. It is obviously intended to appeal equally to lay and to professional readers. The author goes to some pains to deglamorize the wild west as portrayed by Hollywood script writers. Even the illustrations, concentrated in the center of the book, are singularly lacking in glamor. One of the best chapters, written by the author's wife, is also placed in the middle of the book. There is no index, nor is there any need for one.

Recent Progress in the Endocrinology of Reproduction: Proceedings of the Conference Held in Syracuse, New York, June 9-12, 1958. Edited by Charles W. Lloyd. Cloth. $12. Pp. 532, with illustrations. Academic Press, Inc., 111 Fifth Ave., New York 3; Academic Press, Inc. (London) Ltd., 40 Pall Mall, London, S. W. 1, England, 1959.

The purpose of the conference here reported was to bring together basic research as well as clinical investigators to ascertain the continuity of the research and its fruitfulness in the application of everyday understanding of the many facets of reproduction. Most of the work deals with animal experimentation and results, inferences for the most part being applied to human beings. The book presents many observations that are yet to be confirmed either in the laboratory or in the clinic and offers a review of pertinent data as of the time of the conference. This book is primarily for the investigator rather than the practicing physician.

QUESTIONS AND ANSWERS

CONTROL OF LYMPHEDEMA

To the Editor:—*Controversy has arisen in our hospital as to whether the lymphedema of peripheral vascular disease can be more effectively treated with a roller bandage having an elastic weave or with an elastic stocking. Has any controlled study been made of this problem?*

M.D., Illinois.

Answer.—The most important consideration in the use of any device for the treatment of lymphedema is that it be properly fitted to the particular individual on whom it is to be used. The problem with an elastic-weave roller bandage is that it has a tendency to slip and to become uneven soon after it has been applied. It is difficult for most patients to apply their own bandages properly. On the other hand, an elastic stocking frequently is not fitted properly and may be tighter at the top of the leg than at the foot or the ankle. It then has the effect of a tourniquet and completely defeats the purpose for which it is intended. The most effective device for treating lymphedema is a custom-fitted pressure-gradient stocking. With this type of stocking, the pressure is greatest distally and gradually lessens toward the proximal end of the stocking. This is effected by different tensions in the weave. When this stocking is properly fitted, it actually has the effect of a peripheral pump and will greatly facilitate drainage of fluid from an extremity. Custom-measuring is all important. The variance in size and shape of legs results in poorly fitted stockings if they are purchased in a store.

Answer.—I do not know of any controlled study of the problem, but management of lymphedema with peripheral vascular disease of the lower extremity must be divided into early and late stages. In the early stage, neither an elastic-weave bandage nor an elastic stocking is likely to control severe edema. In most instances, a bandage of solid latex rubber must be used during this stage. In the later stage, a combination of elastic bandage and elastic stocking that can be brought up over the thigh in a manner more satisfactory than is possible with a bandage may be required to control edema of both leg and thigh. An elastic stocking is best for supporting the entire lower limb, but in some instances plastic surgery may be required as an adjunct before the edema can be controlled. In every case of lymphedema of peripheral vascular disease of the lower extremity, the principle is that the method of bandaging must be adequate to control the edema.

Answer.—Pratt (*J. A. M. A.* 151:888-891, 1953), in discussing the surgical correction of lymphedema, emphasizes the need for adequate support and believes that this is best obtained by an elastic bandage of suitable compressive strength, since a bandage, unlike a stocking, can be adapted to the changing contours of the leg or arm. Support of this type should be worn until no swelling occurs without it, periods of a year or more often being required. On the other hand, Foley (*Surg. Gynec. & Obst.* 101:25, 1955) recommends elastic stockings. He emphasizes that they should be made to measure and so designed as to start just above the toes and fit snugly, with a compressive force of about 40 mm. Hg in the foot area (a figure which seems high). The compressive pressure must progressively follow a negative gradient in a proximal direction in order to avoid stagnation of blood and lymph in the distal portions of the extremity. Stockings of this type should end below the knee unless edema of the thigh is present, when they should extend well up toward the groin.

A common difficulty is that many types of stockings tend to crease and fold in the popliteal area, creating a tourniquet effect, especially on walking. Recently a type of stocking has been introduced which to some extent obviates this difficulty. Long stockings should always be supported by a belt rather than any type of constrictive garter band. Wilkins and associates (*New England J. Med.* 246:360, 1952) also feel that elastic stockings are useful therapeutically and are safe if not applied at a compressive pressure in excess of 10 to 15 mm. Hg. Litter (*M. Clin. North America* 36:1039, 1952), who studied the hydrodynamics of the problem in detail, also stresses the importance of the compressive strength factor and points out that a critically optimum pressure is required to obtain maximum linear velocity of flow through the veins.

Elastic stockings of the so-called tubular knit type should be avoided, because it is physically impossible to provide suitable pressure gradients with this type of construction. Other stockings of various compressive strengths and designed to provide correct pressure gradients are available but at best represent a compromise with respect to any given extremity, even when offered in a multiplicity of sizes. Furthermore, elastic stockings should not be used over a dressing, since undue pressure is exerted on the dressing and underlying tissues and a tamponade or blocking effect is created. On the

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other hand, elastic bandages are readily applied over dressings so as not to exert undue pressure at any one point and to conform to the contours of the extremity; the tension can be so adjusted during application as to obtain any degree of support required. They are available in a wide range of fabrics and constructions, with or without rubber, so that the proper type of bandage can readily be selected for any given case.

In general, a suitable elastic bandage is to be preferred for postoperative use and for wearing at home, because of ready adaptability to individual factors and inherent physiological efficiency. The danger of too tight application by the patient seems to be minimal. Properly designed and fitted elastic stockings are suitable for temporary use when esthetic considerations are of importance, and they have been found most helpful in minimizing the fatigue encountered by the surgeon during the course of prolonged operations.

SATURATED AND UNSATURATED FATS

To the Editor:—*What is the proportion of saturated and unsaturated fatty acid in butter, commercial oleomargarine, and Emdee?*

M.D., Connecticut.

Answer.—A recent publication of the United States Department of Agriculture, Human Nutrition Division, entitled "Fatty Acids in Food Fats," states that the total saturated fatty acid content of butter, margarine, and Emdee is 55, 26, and 12.7 Gm. per 100 Gm., respectively, and total linoleic acid content is 3, 9, and 35.6 Gm. per 100 Gm. respectively. According to information available at the present time, there is no indication that there should be a headlong rush to change the fat intake of everyone. Where there is a history of heart attacks, the physician may wish to incorporate into the diets of such patients fats with a relatively high degree of unsaturation. Several commercially available products are made with fats such as corn oil, safflower oil, and soybean oil.

LOCATION OF ANOXIC BRAIN DAMAGE

To the Editor:—*A patient's heart stopped beating for 22 minutes during an operation and was resuscitated. There is a considerable amount of marked brain damage. Is there literature available on the part of the brain first affected in such a case?*

Frank A. Andrews, M.D., Coldwater, Mich.

Answer.—Clinical experiences with temporarily interrupted cardiac function and heartbeat with survival of the patient have been recorded for a great many years. There are many factors that will determine the degree of brain injury which follows such an episode. If the patient's body temperature is at normal or above, four to five minutes of complete cardiac arrest is sufficient to destroy the function of the large ganglion cells, particularly those of the cortex. Persons surviving this type of episode usually vegetate or manifest the symptoms of decerebrate rigidity.

The difficulty with human clinical observation is that the exact time of complete cardiac arrest is hard to determine. Some instances of fibrillation and "pulselessness" have been mistaken for complete cardiac failure. The situation then becomes one of differentiating between severe states of cerebral hypoxia and those of true cerebral anoxia. In the human being, four to five minutes of complete anoxia is considered sufficient to greatly endanger intelligent mental reactive processes subsequent to the episode. The age of the patient, infant or adult, is also important. If the patient, however, is subjected to generalized hypothermic situations, the period of cardiac arrest, with recoverable brain function, can be extended well beyond the critical period, depending on the physical factors of oxygen availability, Boyle's law of gases in solution, and the efficiency of the circulation that remains.

The question does not contain information relative to the patient's age, physical state, or body temperature, nor the method of exact measurement of the 22-minute interval involved in the heart-failure mechanism. Was there a preceding peripheral circulatory failure, or was this incident due to sudden total cardiac arrest? What happened to the respiration rate? Were manual, mechanical, or drug agents used in the resuscitation efforts? Assuming that the question involves an operation on a patient not under hypothermic conditions, survival would be most unusual after a 22-minute cardiac arrest unless oxygen reached the cortical midbrain and medulla areas by some means. "Pulselessness," vasomotor failure in the periphery, or fibrillation might have filled in part of the interval.

There is much in recent aviation physiology that indicates that unfavorable degrees of cerebral hypoxia begin to manifest failure at the level of judgment and the frontal lobes. The portions of the brain that show loss of function next are the perceptive areas concerned with the accuracy of vision and hearing, memory recall, and sensation. In gradually increasing degrees of hypoxia, failure of function finally includes the motor and other cortical areas. Because of the "end-artery" system to the basal ganglions, intense local changes may take place and leave coordination and cybernetic factors greatly disturbed. The inference, therefore, would be that the damage should be greatest in the frontal and temporal areas of the brain, along with visual perception, if such clinical tests could be carried out. Where sufficient anoxia has occurred to damage large areas, it is impossible to determine which areas are first affected, since the process is so rapid. The end-point is the same, in that damage is widespread after five minutes of complete cardiac arrest, chiefly in the large ganglion cell areas of the brain cortex, representing the most recent phylogenic additions. Regeneration or recovery of mental acuity does not eventually take place.

WASHINGTON NEWS

Federal Poliomyelitis Report . .
State Activities on Aging . .

POLIOMYELITIS STRIKES LOW INCOME GROUPS

A marked shift in the pattern of poliomyelitis was reported by the U. S. Public Health Service, which said the disease now occurs most frequently in small, crowded areas with heavy concentrations of low socioeconomic groups. There is a substantially higher attack rate among the nonwhite population.

Before the Salk vaccine was widely distributed, poliomyelitis spread over large areas and attacked all population and economic groups, PHS noted.

The nationwide paralytic attack rate in 1959 was 1.6 per 100,000 persons. In the white population the rate was 1.4 per 100,000, compared with 3.2 for nonwhite groups.

In prevaccine epidemics the attack rate was relatively high among older children and young adults, but during 1958 and 1959 children under 5 years of age were the principal victims.

Almost 90% of all cases of poliomyelitis in the nation in the past two years occurred among persons under 30 years of age. However, a few communities in Massachusetts and Seattle, Wash., reported a higher proportion among older age groups.

Children aged under 5 accounted for 37.6% of all cases this year. More than 50% of children aged under 5 have not been vaccinated.

U. S. Surgeon General Leroy E. Burney pointed out that, as in prevaccine days, poliomyelitis continues to follow a cycle with years of high and years of low incidence. Both 1958 and 1959 were years of high incidence. A total of 4,245 paralytic cases was reported for this year through Oct. 9, compared with 2,089 in the corresponding weeks of 1958. In 1955, the first year the Salk vaccine became generally available, there were 8,290 cases during the same period.

The weekly incidence was falling off in October from the peak 332 cases registered in mid-September. The rate for the latest week fell to 229 paralytic cases, 50 fewer than the previous week.

The Salk vaccine has continued to prove "highly effective" in the vaccinated population, said Dr. Burney. Among 3,173 persons with paralytic cases whose vaccine status had been reported by Oct. 5, there were 551 who had had the full course of three or more injections. Of the paralytic cases, 82.6% were among the unvaccinated or partially vaccinated, with 64.2% of these having received no vaccine and 18.5% only one or two injections.

The number of fully vaccinated persons in June was about 68 million. About 36 million persons in the vulnerable under-40 age group had no vaccination at all, and around 5 million of these were infants and preschool children.

Since then, about 25 million doses of vaccine have been distributed in this country, sufficient to increase the number of persons who have had at least three injections by about 18 million.

Fifty-four cities this year conducted surveys to learn who the unvaccinated persons were. The findings reinforced experts' opinion that concentrated vaccination drives must be conducted among certain groups and in certain areas if poliomyelitis is to be controlled, PHS said.

STATES MOVE ON AGING PLANS

The government reported that the states are making progress in preparations for the White House Conference on Aging to be held in January, 1961.

State plans "cover broad and varied programs," said the Department of Health, Education and Welfare in a report on the states' activities.

The report declared that "development of these plans has involved participation by large numbers of private citizens, by representatives of public and private agencies and organizations and official state agencies on aging."

Through September, 35 states and the District of Columbia had received grants from HEW to help finance their aging activities. Total amount of the grants was $514,200.

The latest nine grants, all for the maximum $15,000, went to California, District of Columbia, Kansas, Minnesota, New York, Ohio, Oklahoma, South Dakota, and Tennessee.

The White House Conference is scheduled to make recommendations in all phases of aging problems and to serve as the springboard for concerted community action.

PERSONNEL

Six American scientists studied the progress of metabolic disease research in Russia during September for the Department of Health, Education, and Welfare. They were Drs. Floyd S. Daft, director, National Institute of Arthritis and Metabolic Diseases; William Castle, professor of medicine, and head, department of medicine (Harvard), of

(Continued on next page)

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Riseman, J. E. F., *et al.*: Circulation *17*:22, 1958

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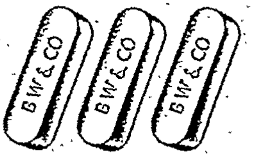


Boston City Hospital; William H. Sebrell Jr., director, Institute of Nutrition Sciences, School of Public Health and Administrative Medicine of the Faculty of Medicine, Columbia University; J. Murray Luck, professor, department of biochemistry, Stanford University; Currier McEwen, associate professor of medicine, New York University College of Medicine; and Clifford J. Barborka, associate professor of medicine, Northwestern University Medical School.

Dr. Pearce Bailey, director of the National Institute of Neurological Diseases and Blindness for the past eight years, was appointed director of the institute's new International Neurological Research Programs. Dr. Richard L. Masland, now assistant director, will succeed Dr. Bailey as director of the institute.

Dr. E. M. K. Geiling, professor of pharmacology at the University of Chicago, has been appointed to the scientific staff of the Food and Drug Administration. He will serve as medical officer and head of the Pharmacodynamics Branch of FDA's Division of Pharmacology.

Dr. Kenneth W. Chapman, associate director of the clinical center of the National Institutes of Health, died in Washington, D. C., of a heart attack, on Sept. 18, while undergoing a physical examination. He was 48 years of age.

Twenty additional persons were appointed to the Advisory Committee to the White House Conference on Aging, raising the total membership to 146. Among those named were Dr. Vincent P. Carroll, Laguna Beach, Calif., professor of clinical surgery, graduate school of the College of Osteopathic Physicians and Surgeons; J. Douglas Coleman, New York, vice-president of the Blue Cross Association; Walter Foody, Chicago, vice-president of the Continental Casualty Insurance Company and currently in charge of the actuarial department and independent plans division underwriting the insurance program for persons aged 65 and over; and Dr. Donald H. Stubbs, Alexandria, Va., chairman of the board of directors of National Blue Shield.

MISCELLANY

A management consulting firm recommended increasing the manpower of the Food and Drug Administration, in view of the growing demands resulting from the development of new products and manufacturing processes. The firm, McKinsey & Co., concluded that FDA is effectively organized to carry out its responsibilities and made a number of proposals for strengthening FDA's inspection, testing, and regulatory activities.

The Public Health Service's division of general medical sciences awarded 98 new grants totaling $3,461,700 to support training programs for research scientists in 11 basic medical and health-related sciences. The grants are part of a National Institutes of Health effort to stimulate more research training, with emphasis on training in the scientific fields basic to medicine and public health.

Scientists at the North Little Rock, Ark., Veterans Administration hospital and the University of Arkansas Medical Center have indicated a possible relationship between virus illnesses in infants and mental retardation later in their lives. Virus infec-

The American Cancer Society awarded the Department of Agriculture $100,000 to intensify research on avian leukosis, a cancerous disease of chickens. Poulty cancers cannot be transmitted to man, but "any significant findings on poultry cancer may be adaptable to human cancer research," said the Agriculture Department.

The Public Health Service awarded 5,262 training grants, research fellowships, and traineeships, totaling $61,900,000, through the National Institutes of Health in the fiscal year that ended June 30. A detailed accounting of these awards for advanced training in medicine and biology is contained in a new publication—"Public Health Service Grants and Awards by the National Institutes of Health, Fiscal Year 1959, Part II." Copies may be obtained from the Superintendent of Documents, U. S. Government Printing Office, Washington 25, D. C. Ask for PHS Publication No. 701, Part II. The price is 40 cents.

President Eisenhower signed into law a bill permitting the dispensation of paregoric by oral as well as written prescription in the District of Columbia.

The lead content of gasoline could be raised from 3 to 4 cc. per gallon without significantly increasing the public health hazard from auto exhausts, according to a special committee of advisors to the Public Health Service. But Dr. Leroy E. Burney, PHS surgeon general, urged that recommended precautionary measures be taken if the gasoline industry does increase the lead content.

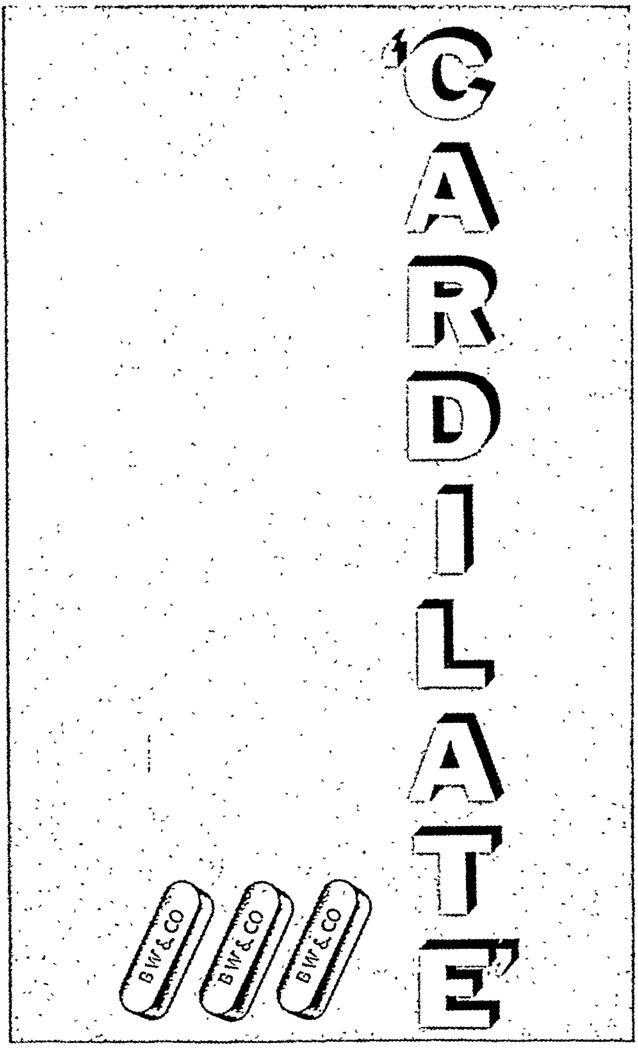
Sen. George A. Smathers (D., Fla.) proposed that the Senate Small Business Committee investigate prices of medicaments and drugs. He said some United States drug manufacturers are selling their products abroad at much lower prices than in this country.

The Atomic Energy Commission consolidated its health and safety programs in a newly created office of health and safety under Dr. Forrest Wester, who has been assistant director for radiation protection in the division of biology and medicine. The new office took over the duties and personnel of the three branches of health and protection, radiation effects of weapons, and safety and fire protection.

Despite various scientific reports on smoking and health, Americans will smoke a record 465.9 billion cigarettes this year, the Agriculture Department predicted. The agency said almost one out of every two Americans over 14 years of age now smokes "regularly."

Roger W. Jones, chairman of the Civil Service Commission, urged 100% employee participation in the newly enacted federal employees' health insurance program. He suggested that workers continue their present health policies until the new program becomes effective next July 1. The CSC chairman termed the program, endorsed by the American Medical Association, "a highly significant addition to the attractiveness of federal employment."

Also published by the Ways and Means Committee was a 220-page book of facts about the administration of the disability provisions of the social security program. The report reviews the legislative history of the disability program, amendments, court decisions, and other statistical information. It was designed for the use of a special ways and means subcommittee, headed by Rep. Burr Harrison (D., Va.), that is slated to hold hearings starting in October on the disability program's operations.



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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

October

American Psychiatric Association, Detroit Divisional Meeting, Hotel Statler, Detroit, Oct. 29-31. Dr. Benjamin Jeffries, 16321 Mack Ave., Detroit 24, Co-Chairman, Planning Committee.

American Society of Tropical Medicine and Hygiene, Claypool Hotel, Indianapolis, Oct. 28-31. Dr. Rolla B. Hill, 3575 St. Gaudens Road, Miami 33, Fla., Executive Secretary.

Congress of Neurological Surgeons, Americana Hotel, Miami, Fla., Oct. 28-31. Dr. Richard L. DeSaussure, Suite 101 B, 20 S. Dudley St., Memphis, Tenn., Secretary-Treasurer.

November

Academy of Medicine of Cleveland Seminar on Recent Advances in Diagnosis and Therapy of Malignant Disease, Cleveland, Nov. 18-19. Dr. H. S. Van Ordstrand, 2009 Adelbert Rd., Cleveland 6, Chairman.

American Academy for Cerebral Palsy, Statler Hilton Hotel, Los Angeles, Nov. 30-Dec. 2. Dr. Glidden L. Brooks, Brown University, Providence 12, R. I., Secretary.

American Association of Blood Banks, Edgewater Beach Hotel, Chicago, Nov. 4-7. Dr. John B. Alsever, Southwest Blood Banks, 1211 W. Washington St., Phoenix, Ariz., Secretary.

American Clinical and Climatological Association, The Homestead, Hot Springs, Va., Nov. 2-4. Dr. F. Tremaint Billings, 420 Medical Arts Bldg., Nashville, Tenn., Secretary.

American College of Chest Physicians, Dallas, Texas, Nov. 29-30. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Secretary.

American Fracture Association, Roosevelt Hotel, New Orleans, Nov. 1-5. Dr. H. W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Executive Secretary.

American Medical Women's Association, Arlington Hotel, Hot Springs, Ark., Nov. 12-15. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

Association of American Medical Colleges, Edgewater Beach Hotel, Chicago, Nov. 2-4. Dr. Ward Darley, 2530 Ridge Ave., Evanston, Ill., Executive Director.

Association of Military Surgeons of the United States, Mayflower Hotel, Washington, D. C., Nov. 8-11. Lt. Col. George M. Beam, AUS, Ret., Suite 718, New Medical Bldg., 1726 Eye St., N. W., Washington 6, D. C., Executive Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Nov. 6-7. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Cleveland 6, Secretary.

Chicago Heart Association, Symposium on Cerebral Vascular Diseases, Knickerbocker Hotel, Chicago, Nov. 7. Dr. C. Bruce Taylor, c/o Chicago Heart Assn., 22 W. Madison, Chicago 2, Chairman.

Conference on Electrical Techniques in Medicine and Biology, Sheraton Hotel, Philadelphia, Nov. 10-12. Dr. Herman P. Schwan, Moore School of Electrical Engineering, University of Pennsylvania, Philadelphia, Chairman.

District of Columbia, Medical Society of, Statler-Hilton Hotel, Washington, D. C., Nov. Mr. Theodore Wiprud, 1718 M Street, N. W., Washington 6, D. C.

Gastroenterology Research Group, Drake Hotel, Chicago, Nov. 6. For information write Dr. Charles F. Code, Mayo Clinic, Rochester, Minn.

Gerontological Society, Inc., Statler Hotel, Detroit, Nov. 12-14. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Administrative Secretary.

Illinois Academy of General Practice, Morrison Hotel, Chicago, Ill., Nov. 9-12. Dr. H. Marchmont-Robinson, 14 E. Jackson Blvd., Chicago 4, Executive Secretary.

International College of Surgeons, Second Western Regional Meeting, Stardust Hotel, Las Vegas, Nev., Nov. 22-24. Dr. F. M. Turnbull Jr., 1930 Wilshire Blvd., Los Angeles 57, Secretary-Treasurer.

Inter-Society Cytology Council, Statler-Hilton Hotel, Detroit, Nov. 19-21. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secretary-Treasurer.

Interstate Postgraduate Medical Association of North America, The Palmer House, Chicago, Nov. 2-5. Mr. Roy T. Ragatz, Box 1109, Madison 1, Wis., Executive Secretary.

Michigan Academy of General Practice, 13th Annual Fall Postgraduate Clinic, Sheraton-Cadillac Hotel, Detroit, Nov. 11-12. Dr. F. P. Rhoades, 970 Maccabees Building, Detroit 2, Convention Manager.

National Proctologic Association, Chicago, Nov. Dr. George E. Mueller, 59 E. Madison, Chicago 2, Secretary.

National Society for Crippled Children and Adults, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

Omaha Mid-West Clinical Society, Civic Auditorium, Omaha, Nov. 2-5. Mrs. Reta M. Crowell, 1031 Medical Arts Bldg., Omaha 2, Execu-

Radiological Society of North America, Inc., Palmer House, Chica Nov. 15-20. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse N. Y., Secretary-Treasurer.

San Diego Academy of General Practice, Hotel Riviera, Las Veg Nev., Nov. 12-14. For information write: Dr. Harold Peterson, 59 El Cajon Blvd., San Diego 15, Calif.

Society for the Scientific Study of Sex, Barbizon Plaza Hotel, Ne York City, Nov. 7. Mr. Robert V. Sherwin, Suite 704, 1 E. 42nd St New York 17, Executive Secretary.

Southern Medical Association, Atlanta, Nov. 16-19. Mr. V. O. Fost 2601 Highland Ave., Birmingham 5, Ala., Executive Secretary-Treasur

Southern Thoracic Surgical Association, Edgewater Gulf Hotel, Edge water Park, Miss., Nov. 19-21. Dr. Hawley H. Seiler, 517 Baysho Blvd., Tampa 6, Fla., Secretary.

Southwestern Medical Association, Roswell, N. M., Nov. 5-7. Dr. Russell L. Deter, 1501 Arizona St., El Paso, Texas, Secretary.

Western Surgical Association, The Broadmoor, Colorado Springs, Co Nov. 19-21. Dr. John T. Reynolds, 612 N. Michigan Ave., Chicago Secretary.

December

American Academy of Dermatology and Syphilology, Palmer Ho Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bl Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morri Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York C Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, S retary.

American Rheumatism Association, Henry Ford Hospital, Det Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New Y 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masseli 700 W. 168th St., New York 32, Secretary-Treasurer.

First Annual Graduate Medical Education Conference-Reside Training Program, Univ. of Pennsylvania, Philadelphia, Dec. Dr. Alfred S. Frobese, Graduate School of Medicine, U. of Pennsylva Philadelphia 3, Chairman.

Medical Society of the United States & Mexico, Valley Ho Ho Scottsdale, Ariz., Dec. 2-4 (followed by two-day session Desert Las Vegas, Nev.). Dr. A. H. Tallakson, 2025 N. Central Ave., Phoe Ariz., Convention Co-Chairman.

New York Heart Association, Symposium on Salt and Water Meta lism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishm N. Y. Heart Association, 10 Columbus Circle, New York City, Chairm

New York State Society of Anesthesiologists, Inc., Postgradu Assembly in Anesthesiology, Hotel New Yorker, New York City, 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secret

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywo by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwau St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer Ho Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicag Executive Secretary.

American College of Surgeons, *Sectional Meeting, the Brown H* Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saund 40 E. Erie St., Chicago 11.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. J R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Execu Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secret

Western Society for Clinical Research, Carmel-by-the-Sea, Ca Jan. 28-30. Dr. William N. Valentine, U. of California Medical Cen Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. Ge Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Mi cine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harb Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tov Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, I 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Execu Director.

American College of Surgeons, Sectional Meeting for Surgeons Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information wr Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chica Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York Executive Secretary.

California Medical Association, Ambassador Hotel, Los Angeles, F 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Execut Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18- Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Cana Secretary.

Congress on Medical Education and Licensure, Palmer House, C cago, Feb. 7-9. For information write: Council on Medical Educati

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STUDIES ON LIVE POLIOVIRUS VACCINE

ITS NEUROTROPIC ACTIVITY IN MONKEYS AND ITS INCREASED NEUROVIRULENCE AFTER MULTIPLICATION IN VACCINATED CHILDREN

Joseph L. Melnick, Ph.D., Matilda Benyesh-Melnick, M.D.
and
James C. Brennan, M.D., Houston, Texas

Comparative tests of the monkey neurovirulence of the Lederle-Cox and the Sabin strains of poliovirus, which are candidates for an orally administered vaccine, have indicated that children have been fed poliovirus strains possessing greater neurotropic activity than had been suspected. There was also evidence that, in passing through human hosts, some of the vaccine strains underwent genetic changes with respect to at least two properties in tissue culture, namely, the capacity to grow at 40 C (T marker) and the capacity to grow at low bicarbonate concentration (d marker). These changes after human passage were associated with increases in monkey neurovirulence. A further study of 596 postvaccination fecal specimens revealed that marked, though not complete, interference occurred between the vaccine virus and the enteroviruses already circulating in the population. This interference affected adversely the formation of the desired antibodies. It has not been proved that the strains used as orally given vaccine are dangerous either for the vaccinated child or for the community, but caution is called for, especially in view of the genetic instability of the attenuated strains of poliovirus currently available.

THE problems of the neurovirulence, genetic stability, and immunizing capacity of live poliovirus vaccines have been brought into sharper focus by the large-scale trials being conducted in different parts of the globe, as recently reported before the Pan American Health Organization–World Health Organization (PAHO-WHO) Conference on Live Poliovirus Vaccine held in Washington, D. C., during the week of June 22-26, 1959. We are summarizing here the results of our recent work on (1) comparative tests of the monkey neurovirulence of the Lederle-Cox strains and the Sabin strains being used as orally given vaccine, (2) the use of the *d* and *T* markers in tissue culture for determining genetic changes in attenuated poliovirus, (3) the correlation between genetic instability and increase in neurovirulence of strains after multiplication in the human alimentary tract, and (4) the limited immunizing capacity of attenuated poliovirus in an area with a high rate of enterovirus infection, presumably due to interference by the latter.

In addition, we would call attention to the fact that the feeding of a large number of persons does not, by itself, constitute an adequate safety test. Two questions must be asked in each field trial: 1. What percentage of those fed had already been immunized by prior natural exposure to poliovirus or by Salk vaccination? 2. Is there a significant difference in the number of cases of poliomyelitis among the vaccinated susceptible persons and their community contacts as compared with the number

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From the Department of Virology and Epidemiology and the Department of Pathology, Baylor University College of Medicine.

of cases which might have been expected had the same population been exposed to a virulent strain of virus? Some data illustrating this approach will also be discussed.

Materials and Method

Monkey Neurovirulence of Vaccine Strains.—Strains were made available through the kindness of Drs. A. B. Sabin and H. R. Cox. They were transported on Dry Ice and kept frozen until the day they were thawed and titrated in monkeys and in monkey-kidney cultures. From 22 to 26 monkeys were used for titrating each strain intracerebrally (IC) and from 22 to 43 for each strain intraspinally (IS). The IC dose was 1 ml. into the thalamus, with use of a 22-gauge needle; the IS dose was 0.1 ml. inoculated into the lumbar cord through the first intervertebral space below the last rib, with use of a 27-gauge needle. The latter was used in order to retain as much as possible of the 0.1-ml. inoculum in the lumbar cord. As a measure of a proper inoculation we sought to obtain continuous reflex contractions of the leg muscles during the inoculation. In order to achieve this, it was necessary, in many monkeys, to change the location of the needle during the course of injecting the vaccine.

TABLE 1.—*Comparative Titrations for Neurovirulence of Type 1 Candidates for Orally Given Poliovirus Vaccine*[*]

		Monkeys Which Received Lederle-Cox Strain		Monkeys Which Received Sabin Strain	
Route of Inoculation	Concentration of Tissue-Culture Fluid	Developing Weakness or Paralysis of Poliomyelitis[†]	Developing Cord Lesions of Poliomyelitis	Developing Weakness or Paralysis of Poliomyelitis[†]	Developing Cord Lesions of Poliomyelitis
Intracerebral..	Undiluted	3/11[‡]	6/11	0/12	1/12
	10^{-1}	1/7	4/7	1/7	1/7
	10^{-2}	4/8	8/8	1/7	1/7
Intraspinal....	Undiluted	8/9	9/9	8/10	10/10
	10^{-1}	3/6	6/6	4/5	4/5
	10^{-2}	5/5	5/5	5/6	6/6
	10^{-3}	4/4	4/4	2/4	3/4
	10^{-4}	5/5	5/3	0/5	3/5
	10^{-5}	0/6	0/6		
	10^{-6}	0/5	0/5		

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[*] Of 46 control monkeys inoculated intracerebrally and 28 inoculated intraspinally, none developed disease or lesions.

[†] Progressive weakness or paralysis beyond second day after inoculation.

[‡] Numerator = number of monkeys positive; denominator = number of monkeys inoculated.

TABLE 2.—*Comparative Titrations for Neurovirulence of Type 2 Candidates for Orally Given Poliovirus Vaccine*

		Monkeys Which Received Lederle-Cox Strain		Monkeys Which Received Sabin Strain	
Route of Inoculation	Concentration of Tissue-Culture Fluid	Developing Weakness or Paralysis of Poliomyelitis[*]	Developing Cord Lesions of Poliomyelitis	Developing Weakness or Paralysis of Poliomyelitis[*]	Developing Cord Lesions of Poliomyelitis
Intracerebral..	Undiluted	5/10[†]	10/10	0/10	0/10
	10^{-1}	3/6	6/6	0/6	0/6
	10^{-2}	3/6	5/6	0/6	0/6
Intraspinal....	Undiluted	10/10	10/10	5/8	8/8
	10^{-1}	6/6	6/6	4/5	5/5
	10^{-2}	6/6	6/6	0/5	4/5
	10^{-3}	3/3	3/3		
	10^{-4}	2/4	3/4		
	10^{-5}	0/4	0/4		

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[*] Progressive weakness or paralysis beyond second day after inoculation.

[†] Numerator = number of monkeys positive; denominator = number of monkeys inoculated.

After a period of observation of about four weeks, or less if the monkey was severely paralyzed, the animals were sacrificed and 30 sections of spinal cord were examined, 10 each from the cervical, thoracic, and lumbar areas. Lesions were graded from 1+ to 4+, a maximum score for both hemisections of one level being 8 (gross destruction of nerve cells plus extensive areas of cellular infiltration and perivascular cuffing); thus, the maximum score for the lumbar or cervical area of a monkey would be 80.

The data in tables 1 to 4 are a condensed summary of the titrations in about 400 young cynomolgus monkeys with a range of body weight of from 3 to 5 lb. (1.5 to 2.5 kg.). Each of the strains gave titers in the same range in monkey-kidney cultures, $10^{6.9}$ to $10^{7.5}$ tissue culture doses (TCD$_{50}$) per milliliter, similar to the results reported by Sabin and by Cox. However, marked differences were found between our results in monkeys and those reported by them.

TABLE 3.—*Comparative Titrations for Neurovirulence of Type 3 Candidates for Orally Given Poliovirus Vaccine*

		Monkeys Which Received Lederle-Cox Strain		Monkeys Which Received Sabin Strain	
Route of Inoculation	Concentration of Tissue-Culture Fluid	Developing Weakness or Paralysis of Poliomyelitis[*]	Developing Cord Lesions of Poliomyelitis	Developing Weakness or Paralysis of Poliomyelitis[*]	Developing Cord Lesions of Poliomyelitis
Intracerebral..	Undiluted	3/10[†]	3/10	0/10	0/10
	10^{-1}	2/6	2/6	0/6	0/6
	10^{-2}	0/6	0/6	0/6	0/6
Intraspinal....	Undiluted	8/10	10/10	9/10	10/10
	10^{-1}	6/6	6/6	3/6	6/6
	10^{-2}	6/6	6/6	3/6	6/6
	10^{-3}	4/4	3/4	0/4	2/4
	10^{-4}	1/4	2/4	0/4	0/4

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[*] Progressive weakness or paralysis beyond second day after inoculation.

[†] Numerator = number of monkeys positive; denominator = number of monkeys inoculated.

For type 1, the Lederle material contained more than 300 monkey poliomyelitis doses (MPD$_{50}$) per milliliter by the IC route, and 300,000 MPD$_{50}$ by the IS route (tables 1 and 4), MPD$_{50}$ indicating the dose which produced specific lesions of poliomyelitis in 50% of the inoculated monkeys. (Usually, as shown in table 1, the titer based on lesions was about 0.5 to 1.0 log$_{10}$ units higher than that based on the appearance of paralysis and weakness.) Sabin's strain produced a significant response in only two monkeys by the IC route, but the IS titer proved to be 100,000 MPD$_{50}$ per milliliter. The extent of multiplication is also evidenced by the lesion scores presented in table 4. After IC injection, Lederle's strain produced marked destruction in both the cervical and the lumbar areas, as shown by the high scores of 457 and 649, while Sabin's strain yielded a score of only 24. After IS inoculation in the lumbar area, the Lederle material showed a high degree of activity (lumbar score, 1,597) and spread into the cervical area (score, 844), i. e., ratio of cervical to lumbar scores of 1/2, while Sabin's material showed a lesser but significant spread, with the ratio of cervical to lumbar scores being 123 to 837, or about 1/7. A low ratio, such as 1/7, of cervical to lumbar scores indicates little spread of the virus from the area of injection while a high ratio, such as 1/2, indicates extensive spread of neurovirulent virus to the cervical area.

For type 2, Lederle's strain titered over 300 MPD_{50} per milliliter by the IC route and 200,000 MPD_{50} by the IS route, while Sabin's strain was negative by the IC but had a titer of at least 2,500 MPD_{50} by the IS route (tables 2 and 4). After IS inoculation, Lederle's strain showed a high degree of activity and of spread (ratio of cervical to lumbar scores, 1,009 to 1,778, or about 1/2) in contrast to the relatively low degree of activity and spread of Sabin's strain (ratio of cervical to lumbar scores, 44 to 346, or about 1/8) (table 4).

TABLE 4.—*Comparative Titers of Candidate Strains of Live Poliovirus Vaccine*

Live Poliovirus Vaccine		50% Doses per Ml.					Poliomyelitis Lesion Scores*			
		Monkey Kidney Tissue Culture	Intracerebral Neurovirulence		Intraspinal Neurovirulence		Intracerebral Inoculation		Intraspinal Inoculation	
Type	Strain		Clinical Disease†	Poliomyelitis Lesions	Clinical Disease	Poliomyelitis Lesions	Cervical	Lumbar	Cervical	Lumbar
1	Lederle	$10^{7.3}$	$10^{2.0}$‡	$>10^{2.5}$	$10^{5.6}$	$10^{5.5}$	457	649	844	1,597
	Sabin	$10^{7.8}$	$<10^{0}$	$<10^{0}$	$10^{4.0}$	$10^{5.0}$	0	24	123	837
2	Lederle	$10^{6.9}$	$10^{2.0}$‡	$>10^{2.5}$	$10^{5.0}$	$10^{5.3}$	487	704	1,009	1,778
	Sabin	$10^{7.2}$	Neg.	Neg.	$10^{2.4}$	$>10^{3.4}$	0	0	44	346
3	Lederle	$10^{7.2}$	10^{0}	10^{0}	$10^{4.7}$	$10^{5.0}$	179	232	584	1,259
	Sabin	$10^{7.5}$	Neg.	Neg.	$10^{3.0}$	$10^{4.0}$	0	0	355	850

* Undiluted through 10^{-2} used for calculation of poliomyelitis lesion scores for monkeys inoculated intracerebrally, and undiluted through 10^{-4} for those inoculated intraspinally.

† Paralysis or weakness due to multiplication of poliovirus.

‡ Approximate figures.

For type 3, Lederle's strain contained only 1 MPD_{50} per milliliter by the IC route but had a titer of 10,000 MPD_{50} by the IS route (tables 3 and 4). After IS inoculation, the differences in lesion scores between type 3 strains were less marked than for the other strains, and the degree of spread was also similar, a high ratio of cervical to lumbar scores of about 1/2 being found for both strains: Lederle ratio, 584/1,259; Sabin ratio, 355/850 (table 4).

The marked discrepancies between many of our titrations and those reported by Sabin and by Cox were surprising. It was on the basis of their findings that the WHO Expert Committee on Poliomyelitis[1] in 1957 recommended that strains be used in field trials only if there was a "complete lack of paralytogenic activity on IC inoculation of maximal doses (in excess of 10^7 TCD_{50}) in rhesus or cynomolgus monkeys and only minimal residual neurotropism by spinal inoculation in monkeys—i. e., only rare development of localized, nonprogressive paralysis in monkeys receiving doses of 10^6 TCD_{50} or more." Our results with both Sabin's and Lederle's strains have since been confirmed by a second impartial laboratory, the Division of Biologics Standards, National Institutes of Health.[2]

In criticizing our results, Sabin[3] implied that we produced so much nonspecific damage in the monkeys that the inoculation procedure and the retention of the inoculum in the cord might have been responsible for the paralytic manifestations. A series of control tests with normal tissue-culture fluids, with an enteric cytopathogenic human orphan (ECHO) virus, or with the vaccine strains diluted beyond their paralytogenic end-point, failed to produce disease or histological responses that in any way could be confused with those of poliomyelitis.

Our results indicate that children have been fed poliovirus strains possessing greater neurotropic activity than had been suspected, the degree of which is shown in table 5. (The same may be said for children fed Koprowski's strains, in view of the high degree of neurotropic activity found in these strains by Sabin[3] and by the Division of Biologics Standards.[2]) We have considered 0.01 ml. of infectious tissue-culture fluid, containing 10^5 TCD_{50}, as the dose generally used for human feeding with Sabin's strains, and 10^5 to 10^6 TCD_{50} as the dose with Lederle's strains. Thus one human dose of virus, the amount used to produce infection in the vaccinated child, contains from 100 to 30,000 poliomyelitis doses for the monkey inoculated by the sensitive intraspinal route.

Use of Tissue Culture Markers for Determining Genetic Changes in Attenuated Poliovirus.—Within the past two years, at least three markers of poliovirus have been described which can be followed by tissue culture methods and which tend to discriminate between neurovirulent and attenuated strains. Strains possessing the *d*+ marker grow more rapidly than *d*− strains at low bicarbonate concentration under agar[4]; strains possessing the *MS*+ marker grow more rapidly on the monkey stable kidney-cell line than *MS*− strains[5]; strains possessing the *T*+ marker grow readily at 40 C in contrast to the *T−* strains.[6] Virulent, wild strains possess *d+*, *MS+*, and *T+* markers and thus differ from most attenuated strains.

In the course of a study of a number of families in Mexico City who had been fed Sabin's attenuated strains in the spring of 1958, Ramos-Alvarez kindly made available to us serial specimens of rectal swabs from 81 vaccinated children and their family contacts. The details of the study and of the methodology will be reported separately. Here we wish to point out the usefulness of the method in being able to select, for the expensive monkey-neurovirulence tests, strains which have altered after multiplying in the human alimentary tract. In table 6 the results on 36 strains recovered from vaccinated children show that in 15 there was no detectable alteration in the virus, in 16 others the recovered virus changed in the *d* but not in the *T* marker, and in 5 others changes occurred in both markers. Thus, in 14% of the children infected with *d−T−* strains, the excreted viruses had changed in at least two properties. When a strain reverted from *d−* to *d+*, it was not always associated with a *T−* to *T+* reversion. However, every instance of *T−* → *T+* reversion was linked with a *d−* → *d+* reversion.

Table 5.—*Amount of TCD$_{50}$, MPD$_{50}$ (IC), and MPD$_{50}$ (IS) in One Human Dose of Live Poliovirus Vaccine*[*]

Vaccine Strain		TCD$_{50}$	MPD$_{50}$(IC)	MPD$_{50}$(IS)
Lederle	1	10^{5}-10^{6}	$10^{0.5}$-$10^{1.5}$	$10^{3.5}$-$10^{4.5}$
	2	10^{5}-10^{6}	$10^{0.5}$-$10^{1.5}$	$10^{3.3}$-$10^{4.3}$
	3	10^{5}-10^{6}	0	$10^{3.0}$-$10^{4.0}$
Sabin	1	$10^{5.3}$	0	$10^{3.0}$
	2	$10^{5.2}$	0	$>10^{1.4}$
	3	$10^{5.5}$	0	$10^{2.0}$

[*] MDP$_{50}$ indicates dose producing specific poliomyelitis lesions in 50% of inoculated monkeys; IC = intracerebral and IS = intraspinal route of inoculation.

Correlation Between Genetic Instability and Increase in Neurovirulence.—Strains recovered from the Mexican children fed Sabin's vaccine strains were selected for testing in monkeys. The strains had all been isolated in monkey-kidney cultures maintained in M-E medium at pH 7.4. (The M-E medium used contained 0.5% lactalbumin hydrolysate and 1% monkey serum, in Earle's balanced salt solution.) However, to insure that we were not selectively enhancing the proportion of monkey paralytogenic strains by passage of the human virus in tissue culture, a number of rectal swabs obtained from the vaccinated children were inoculated directly into monkeys by the intraspinal route. The dose of virus in such material which could be inoculated was very small indeed, varying from only 10 to 60 TCD$_{50}$.

A summary of the monkey tests on strains of the 3 types is shown in table 7. It is apparent that excreted strains which retain the *d−T−* markers of the vaccine virus are not significantly more virulent for monkeys than the vaccines themselves, about 10,000 TCD$_{50}$ being required to paralyze 50% of the monkeys inoculated intraspinally, and no illness being produced either by undiluted tissue-culture fluid inoculated intracerebrally or by the rectal swabs inoculated intraspinally. The *d+T−* strains show increased activity, both intraspinally and intracerebrally, when compared to the *d−T−* vaccine virus. Thus, only 10 TCD$_{50}$ of the cultured virus were found to contain one monkey-paralyzing dose$_{50}$ (intraspinal), and some of the strains were also active after intracerebral inoculation. Furthermore, 10 to 60 TCD$_{50}$ of virus in the rectal swabs themselves produced paralysis in a significant number of test monkeys inoculated intraspinally.

The strains which changed in both markers to *d+T+*, showed even greater neurovirulence. One strain (recovered from a 2-month-old vaccinated child) which had reverted to the *d+T+* state, was selected for inoculation not only into monkeys but also into a chimpanzee, as members of this species are known to be much less sensitive to attenuated poliovirus than monkeys. Only 10 TCD$_{50}$ of passage virus, or the same small dose as present in the rectal swab, produced paralysis when inoculated intraspinally in monkeys; in addition, the undiluted passage virus proved to be paralytogenic in monkeys inoculated intracerebrally and also in the chimpanzee inoculated intraspinally.

Cytopathogenic virus was recovered from the spinal cords of almost all monkeys sacrificed soon after the onset of paralysis, indicating that no selection of strictly neurotropic virus had taken place in the central nervous system of the monkeys.

Field Trial

Interfering Effect of Enteroviruses Circulating in a Population on Immunizing Capacity of Attenuated Poliovirus.—In the course of the 1958 family study in Mexico City already referred to above, 596 postvaccination stool specimens were tested. Of these, a total of 237 specimens exhibited a cytopathogenic agent in monkey-kidney cultures. Only 37% were homotypic polioviruses, i. e., polioviruses of the same type as in the vaccine fed, while 57% proved to be enteroviruses other than poliovirus. Table 8 illustrates the interfering effect of the latter on infection with the vaccine viruses and on poliomyelitis antibody formation. Of 28 children who were free of enteroviruses before feeding, 22 developed antibodies against the vaccine virus. Poliovirus was isolated from 18 out of these 22 children. On the other hand, 33 of 47 children excreting other

Table 6.—*Markers of Polioviruses Excreted by Vaccinated Children Orally Infected with Sabin's Attenuated Strains*

Markers of Vaccine Virus Used to Initiate Infection	Poliovirus Types	Viruses Excreted by Vaccinated Children			
		Total Tested	d−T−	d+T−	d+T+
d−T−	1	16	12	4	0
d−T−	2	8	2	6	0
d−T−	3	12	1	6	5
Total		36	15	16	5

enteroviruses failed to produce antibodies to the vaccine viruses, and only 3 out of these 33 excreted poliovirus. The interference of the enteroviruses, although marked, was not complete, for the remaining 14 of the 47 children did produce antibodies, and of these 14, 10 excreted homotypic polioviruses in spite of the competing infections with other enteroviruses. The detailed analysis of this study will be reported together with Dr. Manuel Ramos-Alvarez.

Measurement of Degree of Safety of a Vaccine in the Field.—It seems obvious that only susceptible persons should be considered in evaluating the results of a field trial. In the study in Mexico City,[7] the number of children with poliomyelitis antibodies prior to the feeding of vaccine was already 33% in those one year of age, 54% in the 2-year-olds, and 85% in those 3 to 5 years old. Feeding in such a population is significant only if the children under 3 years of age are considered, and even in this population the number of those susceptible is far less than the total number fed. Feeding virus to children having contacts who are chiefly immune by natural infections tells very little about the safety of a vaccine for a community, for the opportunities of spread in immune populations are severely limited. Thus, if 100,000 children 3 to 5 years of age are fed virus, in a population whose natural immunity has reached 85% by this age, the actual "test group" of vaccinees is reduced to only 15,000, and the number of their susceptible contacts is likewise only a small fraction of the population.

Another factor in the evaluation of such studies must be the consideration not only of the number of children fed but also of the number of cases of poliomyelitis expected if the same population had been exposed to virulent poliovirus. In this way an answer can be sought as to how much safer is infection with the vaccine than infection with virulent epidemic poliovirus. At least two kinds of data are available to arrive at such figures.

In the unfortunate experience during 1955, in which live virulent virus escaped inactivation in certain lots of Salk vaccine, a number of paralytic cases occurred among vaccinated children. Two studies, one by the neutralization test[8] and one by the complement-fixation test,[9] indicated that high antibody titers were present in 31 to 40% of children six to eight weeks after receiving a single intramuscular dose of the vaccine containing live virus, in contrast to 1 to 8% in control, nonvaccinated children in the same area, or in children receiving a single dose of properly inactivated Salk vaccine. As 20 type 1 (virulent Mahoney strain) cases of poliomyelitis occurred among 32,000 children vaccinated with the inadequately inactivated lots, the serologic data indicate that the 20 cases occurred among some 10,000 "infected" children, or 1 case per 500 infected. However, the argument might be raised that these children were infected by an unnatural route.

Another approach to this problem has been made by studying the acquisition of [illegible] bodies during a severe type 1 [illegible] us to determine subclinical infection rates.[10] The analysis showed that one paralytic case occurred for approximately 100 children infected with the epidemic virus.

Thus, before any claims of safety can be made with regard to an orally given vaccine, large numbers of children must be used. A study involving only 100 children, even if all are susceptible, would be expected to yield no more than a single case if the virus were of the wild, virulent type. For this reason, small studies involving a few hundred susceptible children, as recently carried out in Minnesota,[11] yield very little evidence of safety; the expected cases, even with virulent virus, would be too few in number to indicate how much safer the vaccine virus is than virulent virus.

TABLE 7.—*Correlation of* d *and* T *Characters of Poliovirus Strains with Monkey Neurovirulence*

				No. of Monkeys with Clinical Poliomyelitis/No. Tested					
				Log TCD₅₀ Inoculated					
		Characters*		Intraspinally				Intracerebrally	Rectal Swab Intraspinally
Strains	No. of Strains Tested	d	T	4.5-4.2	3.5-3.0	2.5-2.0	1.0	7.5-6.2	1.8-1.0
Vaccines fed	3	—	—	8/18	2/8	0/9		0/32	
Viruses excreted	6	—	—		9/11	0/9		0/2	0/6
	1	±	—			2/2			2/2
	8	+	—		2/2	16/16	4/13	2/6	3/9
	2	+	+			4/4	3/4	5/5	2/2†

* d and T characters were each established by repeat tests.

† Of these two strains, material from only one rectal swab was available in sufficient amounts for testing in monkeys. This material possessed the T+ marker. All other rectal swabs were T—. No d character tests were performed with rectal swabs.

Comment

The 1957 report of the WHO Expert Committee on Poliomyelitis[1] lists one of the "criteria which should be fulfilled in the design of carefully controlled field trials," as follows: "It is suggested that the properties of these attenuated strains which can be tested in the laboratory, be measured in a number of different laboratories so that there can be more than one opinion as to their pathogenicity or the lack of it."

Data now accumulating from this and other laboratories[12] indicate serious disagreement with the degree of attenuation claimed for the viruses being fed and also for the degree of reversion being found in the virus which multiplies in, and is excreted by, some of the vaccinated children. We do not imply that we have proved that such virus strains are dangerous either for the vaccinated child or for the community, but we wish to emphasize that the risks appear to be greater than had been suspected and that much more knowledge must be obtained concerning how the viruses may be altered in persons living under different macroclimatic and microclimatic conditions, before the available attenuated strains can be said to meet the criteria of a safe and effective vaccine for the control of poliomyelitis.

The data on monkey neurovirulence presented in our paper, and those of the Division of Biologics Standards,[2] were obtained with a slight refinement in testing methods. They reveal that the orally given vaccines currently in field trial are much more neurovirulent than had been found by the proponents of the vaccine. Indeed, Sabin himself has reported[3] that the Lederle and Koprowski strains in his hands are more neurovirulent than has been reported. In view of these findings, the question of safety has now changed from the one originally posed. Originally, investigators in this field had asked: "Are the attenuated viruses, which are almost free of monkey-neurotropic activity, safe immunizing agents for man?" The question must now be phrased: "How much monkey-neurovirulent activity may a strain safely possess if it is to be used for infecting and immunizing children?" The answers seem to be coming in from the increasingly large-scale tests being carried out on children by many investigators. In the course of these trials, an answer might also be obtained on another uncontrollable factor in the epidemiology of poliomyelitis: Do different microclimates and macroclimates influence virus-host relationships, so that what is safe for the host under certain circumstances may become dangerous if those circumstances change? Virulent and attenuated poliomyelitis strains may circulate year in and year out in communities, conferring a high degree of immunity, with little associated disease, and suddenly paralytic cases may begin to appear in the population. The reasons for the initiation of epidemics have not yet been adequately explained.

Table 8.—*Influence of Infection with Other Enteroviruses Before Attenuated Poliovirus Vaccine Feeding on Homotypic Antibody Production Against Vaccine Virus*

	No. of Children Who Did Not Excrete Other Viruses Before Vaccine Feeding			No. of Children Who Excreted Other Viruses Before Vaccine Feeding		
Antibody Status	Total	Excreted Poliovirus	Did Not Excrete Poliovirus	Total	Excreted Poliovirus	Did Not Excrete Poliovirus
Homotypic antibody rise after feeding	22	18	4	14	10	4
No homotypic antibodies before or after feeding	6	0	6	33	3	30
Total	28	18	10	47	13	34

At this time, it is the question of genetic stability of the vaccine virus which is of primary importance[12] rather than questions of dosage, order of feeding of strains, etc., to which many investigators are giving their attention. Obviously, if one selected random samples from vaccinated children for testing for monkey neurovirulence, one might choose strains which had not altered in the human alimentary tract—particularly if such strains were the predominant ones being excreted. In table 6 it can be seen that only 5 of 36 strains showed reversion in two characters, and it was these markedly altered viruses which showed the greatest reversion in monkey neurovirulence. Not only did they become paralytogenic for monkeys inoculated in large doses by the intracerebral route but as little as 10 tissue culture doses of the reverted viruses were sufficient to produce paralysis in monkeys inoculated by the intraspinal route. It is only these altered viruses in the progeny of the vaccine virus which are apt to be dangerous as they are passed about, under no control, in the community. Whether or not viruses which alter soon after they begin to multiply in man may ever enter the vaccinee's brain and spinal cord is not known. Certainly, judging from the large number of persons who have been given these vaccines, the danger does not appear great. However, until more is known about the factors which turn a harmless carrier into a paralytic patient, this is a feature which cannot be controlled.

At the PAHO-WHO Washington Conference of June, 1959, the comment was made again and again, by proponents of live virus vaccination, that the significance of monkey neurovirulence is not understood. Neurotropic activity for monkeys may not indicate a similar activity for children. However, the criteria for the selection of strains for feeding were based on reduction of neurovirulence for monkeys, and it seems obvious—to us at least—that this character should be established as a stable one before large-scale feeding of live virus is continued. In this regard it is noteworthy that, among Sabin's strains, it was the type 3 which showed the greatest spread within the spinal cord (table 4), and it was this same strain which underwent the greatest increase in monkey neurovirulence after human passage (tables 6 and 7).

The problem of viral interference was mentioned by several investigators (Gelfand, Sabin, Paul, and Gear) at the Washington conference. The enteric tract of a child may be temporarily committed to the production of a nonpoliomyelitis enterovirus, blocking the establishment of infection and immunity by the vaccine virus in as many as 50% of poliomyelitis-susceptible children (table 8). A vaccine with such a low rate of effectiveness, even if safe, would leave much to be desired. Whether increasing the dosage will overcome this viral interference without decreasing the safety margin of the vaccine, as suggested by Cox, remains to be determined by future investigations.

Other problems, on which our experimental data do not bear but which have yet to be met before the attenuated strains can be said to meet the criteria required of human vaccines, are discussed below:

First, the reproducibility of the properties of the vaccine from one lot to the next must be established. Only a single large lot of Sabin's strains has been produced in the United States, although recent work in the U. S. S. R. is now going forward with further "production" lots. How will each lot be tested, not only for residual monkey neurovirulence but also for genetic stability and spread in man? Will separate field trials have to be run with each lot? Can the data obtained from a field trial in one part of the world be used to indicate the safety and potency response in another part of the world, where the children have different bacterial and viral flora in their enteric tracts?

Second, the attenuated poliovirus strains are being prepared in monkey-kidney cultures, which often contain adventitious viral and other agents.[13] One of these, B virus, is known to produce fatal infections in man.[14] It is now eliminated from consideration by testing small portions of a large batch of vaccine, in rabbits. Are enough data at hand to say that a human being is no more susceptible than the rabbit or that testing a small volume of vaccine is enough to insure the absence of this dangerous virus from the entire lot? One should also bear in mind that many other simian viruses exist and that they have been little studied. Their detection may be handicapped by the fact that sensitive and reproducible tests have not yet been developed for many of them. A controversy now exists between Sabin[3] and Koprowski,[15] in which the former claims that a wild simian virus was present in Koprowski strains fed to over 50,000 persons in Africa, Poland, and Sweden.

Summary and Conclusions

Tests in monkeys of the live poliovirus vaccines currently being used in field trials have shown them to be more neurovirulent than was found in the laboratories of the proponents of the vaccines. The range of neurovirulence varied from the least virulent (Sabin's type 2)—which reacted negatively after intracerebral injection but contained at least 2,500 monkey poliomyelitis doses per milliliter after intraspinal injection—to the most virulent (Lederle's types 1 and 2) which contained at least 300 monkey doses per milliliter by intracerebral injection and 300,000 monkey doses per milliliter by intraspinal inoculation. The higher titers found by intraspinal injection seem to hinge on the use of a fine needle and the retention of the virus inoculum within the spinal cord.

The degree of genetic stability of the attenuated poliovirus as it undergoes multiplication cycles in vaccinated children and their contacts is of the utmost importance.[12] The use of tissue-culture markers for monitoring the stability of attenuated strains in the field is illustrated in a study of Sabin's strains fed to children in Mexico City. The excreted viruses which showed the greatest alteration in the tissue-culture *d* and *T* markers also showed the greatest increase in monkey neurovirulence (active after intracerebral injection, and only a few virus particles sufficing to paralyze monkeys after intraspinal injection). One altered strain was tested in a chimpanzee and found to be paralytogenic when inoculated intraspinally. That the increased monkey neurovirulence was not a laboratory artifact, brought on by cultivation of the virus under conditions favoring the growth of virulent particles, is shown by the finding that the few virus particles present in rectal swabs (10 to 60 tissue culture doses) were sufficient to paralyze monkeys inoculated intraspinally.

In the course of the Mexican study, it was found that many serologically susceptible children (i. e., free of poliomyelitis antibody) were resistant to infection by the vaccine. As such children were found to be already excreting a nonpoliomyelitis enterovirus at the time the live poliovirus vaccine was fed, the resistance has been attributed to the current infection with the nonpoliomyelitis enterovirus blocking the implantation of the vaccine virus. Interference of this sort might well limit the effectiveness of an orally given vaccine in areas where enterovirus infections are common.

The question of safety of the live poliovirus vaccine resolves itself on the frequency of disease in vaccinated children and their contacts, as compared with that anticipated from natural infection with wild polioviruses. In measuring the safety and effectiveness of live poliovirus vaccine, field investigators should consider not only the number of children fed but also the number already naturally immune and the number of poliomyelitis cases to be expected if the same population were exposed to virulent virus.

If caution was called for in 1954 and 1955 when the Salk vaccine was introduced into large-scale field use, then caution should also be the watchword now.

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"CONSTITUTIONAL" ALLERGIC REACTIONS AND THEIR PREVENTION

George L. Waldbott, M.D., Detroit

The major occasions for constitutional allergic reactions are intradermal tests with allergens, treatments with antigens, sclerosing injections for varicose veins, local anesthetics, injections of radiopaque mediums for roentgenographic diagnosis, injections of antibiotics and hormones, inhalation of airborne substances, and ingestion of foods or drugs to which the patient is sensitive. Treatment of reactions must be prompt. Epinephrine and a tourniquet are the first standbys. Intradermal tests should be done only on arms and legs where a tourniquet can be applied and not on the back. Penicillin should never be given without a preliminary intradermal test and should not be injected into the hips or trunk where a tourniquet cannot be applied. The danger is lessened by proper timing of injections and by preliminary injection of a small test dose of a drug before the full intended dose is given.

As the name implies, in a "constitutional," "systemic," or "generalized" reaction (excluding delayed reactions of the serum sickness type) the allergic process is not confined to a single shock organ such as the bronchial tree or to the nose and sinuses. It involves practically every organ of the body, notably the skin and the mucous membranes of the respiratory tract. There is, however, a tendency for the allergic reaction to concentrate in a preexisting shock organ.[1] For instance, when a patient with dermatitis develops a constitutional reaction dermal manifestations predominate and in one afflicted with asthma, asthmatic symptoms. An allergic reaction initiated by severe uterine or gastrointestinal spasms after an overdose of pollen extract is relatively rare.

Manifestations

The classic type of reaction [1] begins with tingling and itching in the palate, palms, and genitalia, with sneezing, conjunctival edema, and a dry nonproductive cough. Generalized urticaria and allergic respiratory symptoms, especially bronchial asthma, follow in short order. In severe shock, especially

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From Harper Hospital and Woman's Hospital.

after an intravenous injection, death may occur so precipitously that no symptoms other than collapse are noticeable. This is also true in persons whose sensitivity has been acquired, as, for instance, in some of the fatalities reported from penicillin. Here autopsies reveal petechial hemorrhages and edematous changes in the lung tissue and other vital organs instead of urticaria, bronchospasm, emphysema, and accumulation of mucus in the bronchial tree.[2] It seems that these patients, like animals in anaphylactic shock, do not yet have the ability to react to the sudden influx of the antigen into the system as an asthmatic patient does during a constitutional reaction.

In contrast to a delayed reaction of the serum sickness type the immediate constitutional reactions rarely produce any lasting effects. Indeed, existing allergic symptoms are often controlled temporarily by the reaction. Occasionally, however, a pneumonitis or a sinus infection may ensue, especially when the symptoms have not been promptly controlled.

Causes.—Allergic reactions are caused by injected, ingested, and inhaled antigens. The major occasions for reactions are intradermal skin testing and antigenic treatments; sclerosing injections for varicose veins; injections of local anesthetics or opaque mediums for x-ray studies; antibiotics, vitamins, and gland products, including insulin and ACTH; inhalation of airborne substances; and ingestion of foods and drugs to which the patient is very sensitive.

Of particular concern to general practitioners are reactions from injections of penicillin and ingestion of aspirin tablets. Allergists are most frequently confronted with reactions from therapeutic injections and from intradermal skin tests. Regardless of whether the agent is an organic or inorganic chemical, protein or nonprotein, the symptoms produced are identical.[3] It is true that very small doses may elicit a reaction, but the larger the dose the greater the risk.

Differential Diagnosis.—Various kinds of reactions may follow a hypodermic injection such as febrile reactions from contaminated glass and rubber utensils, a flare-up of a dormant focus of infection, or a pulmonary thrombosis. Such reactions must be differentiated from allergic shock. In our daily practice, however, mainly two conditions give rise to confusion, namely, syncope and the toxic effect from an ingested or injected drug. Syncope can be recognized promptly by bradycardia and pallor of the face as distinguished from tachycardia and flushing of the skin in the allergic reaction.

The vasodilating effect of an intravenous injection of aminophylline, or the toxic action of a local anesthetic in a patient intolerant to the drug, may be confused with an allergic reaction. I have presented[4] clinical and autopsy data on two fatalities occurring after administration of procaine (Novocain) hydrochloride; one appeared to be due to intoxication from an accidental intravenous injection, in a patient debilitated by chronic illness, and the other was probably the result of allergic shock.

Modes of Reactions.—Experience with pollen injections has taught us to distinguish three modes of allergic reaction (see table), namely, from an overdose, from an accidental intravenous injection, and from backseepage.[5]

A reaction from an overdose is initiated by a local edema at the site of injection. This can be seen expanding along the lymph channels before generalized urticaria and respiratory symptoms ensue. In an overdose reaction there is a lapse of a few minutes to an hour or more before generalized symptoms arise. The shorter this time interval the more severe the reaction.

This is in contrast to the immediate onset and immediate climax of a reaction to an intravenous injection, in which there is no local edema. This type of reaction invariably constitutes an emergency.

A backseepage reaction is due to injection of antigen next to and seepage into an accidentally punctured vein. It develops within one to several minutes. A local edema forms rapidly with extensive wheal formation. Blood may appear at the site of the injection, and often a bloody suffusion is present. The reaction is characterized by shock and collapse.

Allergic Reactions from Pollen Injections

	Type		
	Intravenous	Backseepage	Overdose
Incidence[5]	1:9,387	1:1,564	1:308
Onset after injection	10 to 20 sec.	1 to 5 min.	Depends on severity
Local reaction	No	Yes	Yes
Blood at site of injection	Often	Usually	Rare
Use of tourniquet	Ineffective	Effective	Effectiva

Treatment.—In treating an allergic reaction the speed with which medication is administered determines the outcome. The lapse of even a minute can be decisive. Therefore, various therapeutic agents should be available for instant use.

Epinephrine and a tourniquet are our first stand-bys. In intravenous and backseepage reactions doses as large as 1.0 cc. should be given. They may have to be followed up with subsequent doses of 0.5 cc. within a few minutes or at longer intervals to be determined by the patient's response. In the more slowly developing overdose reaction a dose of 0.1 to 0.2 cc. is necessary. It can be repeated several times. A tourniquet[6] applied above the site of the injection in order to slow down absorption of the injected antigen has proved most valuable in the control of both overdose and backseepage reactions. It is useless when the injection has been given into a vein.

Then, if allergic edema predominates, an antihistaminic such as diphenhydramine (Benadryl) hydrochloride, 2 to 5 cc. (20 to 50 mg.), should be administered intravenously. If asthma is the predominant symptom, aminophylline, (0.5 Gm.), should be given intravenously. In severe shock the needle should be kept in the vein, in order to be prepared to give epinephrine intravenously in doses of 0.1 to 0.3 cc. This should be injected slowly, mixed with blood drawn into the needle, in order to minimize the danger of cerebrovascular and cardiac damage from the drug. On two occasions intravenous administration of epinephrine has appeared to be of great benefit after other procedures have failed.

Intermittent positive pressure or the Pulmotor of the fire department have also been of considerable assistance. Respiration can be maintained by forcing oxygen and carbon dioxide into the collapsed and spastic bronchi.

Intravenous administration of steroid preparations is of no avail in the control of an immediate reaction, but therapy with steroids can be given after the other drugs and will undoubtedly enhance the speed of recovery. The value of glucose and of calcium preparations for intravenous administration has not been conclusively demonstrated.

In reactions of minor severity too extensive treatment, especially with epinephrine in oil and antihistaminics, tends to produce more discomfort to the patient than the reaction itself.

Prevention of Constitutional Reactions

The incidence of reactions is proportionate to the caution employed by the physician with respect to hypodermic injections, his conservatism in gauging the doses of antigenic treatment, and the competence of his personnel. Needless to say, epinephrine, a tourniquet, and the other therapeutic agents must always be available for prompt action.

Intradermal Skin Testing.—It is fallacious to assume that preliminary scratch tests are a safeguard against constitutional reactions, which occur in spite of negative results of scratch tests, especially if the testing material employed for the scratch tests has lost its potency because it has been on hand too long. In infants and young children, who are notably more susceptible to reactions than adults, intradermal skin testing should be done sparingly. Instead, the passive transfer method should be employed.

When the patient's history discloses that ingestion or inhalation of a certain antigen has in the past given rise to allergic shock, a C, for "caution," entered on the record for this particular antigen signifies that it must automatically be omitted from intradermal testing. If it becomes necessary to treat the patient for this substance his degree of sensitivity must first be titrated with adequately diluted extracts.

Intradermal tests for antigens to which reactions are known to occur more readily, such as nuts, fish, and beans, should be done last. If the initial tests for other antigens have produced strong positive reactions, and thus indicate a marked sensitivity of the patient, subsequent tests should be omitted altogether or done by the scratch method. Fungi and pollens are well suited for preliminary evaluation of the patient's sensitivity. For use in testing patients with excessive sensitivity, the extracts customarily used should be diluted 1:10 or 1:100.

Intradermal skin tests should be performed only on arms and legs where a tourniquet can be applied and not on the back. One should attempt to avoid superficial veins. The tests should be done in an area where the patient can be constantly observed by the physician or his personnel.

Antigenic Treatments.—Overdose reactions can be prevented by using conspicuous labels to distinguish between various concentrations of extracts; by using syringes of different colors for extracts of high and low concentration; by thoroughly cleansing the syringes before they are sterilized; by conservatively gauging the patient's sensitivity; and by adequately reducing doses when changing to fresh, more potent extracts in cases where a previous overdose reaction has occurred. The patient should be kept in the office for at least 10 minutes after the injection so that the injected site can be inspected for excessive wheal formation. An overdose reaction can be predicted from the appearance of the injected area.

In order to prevent reactions from venipuncture an area between visible veins should be selected for the injection. Before injecting the extract the plunger should be withdrawn for evidence of blood. The site injected should be inspected immediately after the injection for escaping blood, which is sometimes—in venous bleeding—a sign of an imminent reaction. Cotton should be applied with pressure on the area where blood is escaping in order to counter backseepage. Self-administration of antigenic extracts should be prohibited. In spite of all these precautions, however, there is no absolute safeguard against accidental venipuncture.

Use of antihistaminics or epinephrine in conjunction with antigenic treatment has been suggested. However, these agents reduce the local swelling and may be inconsistent in their prevention of constitutional reactions. They may thus interfere with the orderly progress of desensitization, although they do not modify the protective effect of the antigen.

Penicillin Injections.—Because of the ever-increasing number of fatalities from penicillin injection, both reported and unreported, this problem deserves special attention. In allergic patients treatment with penicillin should be avoided whenever other antibiotics can be used instead. If the patient's history reveals a previous reaction to penicillin, of either the serum sickness or the immediate generalized type, it should be employed only in an emergency.

In this case an intradermal skin test with an aqueous solution diluted about 1:100 should precede the injection; if the result is negative this should be followed by the intradermal injection of 0.05 cc. of the penicillin compound, the total dose to be administered 15 minutes later. Previous doses of epinephrine or ephedrine-like drugs, or of antihistaminics, interfere with a positive reaction. Therefore, a negative test result within four to six hours of the use of these drugs is unreliable. Under no circumstances should penicillin be used if the result of a skin test is positive; i. e., if it exhibits a definite wheal formation. Even if the result is negative, the penicillin injection should be preceded by an injection of an antihistamine and/or epinephrine. This precaution is likely to reduce the severity of an anaphylactic reaction, but it will not prevent it.

In less urgent cases careful testing, by titration, of the patient's sensitivity and systematic short-interval hyposensitization with very weak dilutions should precede its administration. The principle of this treatment and its technique, originated by Freeman,[7] has been outlined elsewhere.[8] A dilution of an aqueous solution of penicillin low enough to induce only a medium-sized wheal is injected intradermally. The doses are then carefully increased every one to three hours in such a manner that only local reactions of a moderate degree result. The success of this treatment depends on (1) starting with a low enough dose to produce only a small local wheal at the site of the injection, and (2) discontinuing the injections for at least four hours at any time when the local edema appears to be excessive or when a generalized reaction threatens. Whereas I have had considerable experience with this method in diminishing sensitivity to other antigens, I have employed it in only two asthmatic patients in whom penicillin had previously induced generalized reactions. Positive intradermal reactions were obtained with an aqueous dilution of penicillin of 1:10,000 (3 units) and 1:1,000 (30 units) respectively. In one of the patients a dose of 300,000 units of aqueous penicillin could be administered after three days; in the other this dose could be given after five days.

Penicillinase is not likely to be of assistance in treating an immediate reaction from penicillin. Penicillin should not be injected into the hips or trunk where a tourniquet cannot be applied. Inspection of the patient's arm 10 minutes after an injection is a precaution that cannot be too strongly emphasized.

In my experience a time interval of 10 days to six weeks between one injection and another appears to be more conducive to the development of penicillin sensitivity than injections given daily or every second or third day. In other words, the history of injections having been given from 10 days to six weeks previously calls for greater caution. In experimental anaphylaxis the optimal interval between the sensitizing and shocking injection is between 10 and 20 days.

Inhaled and Ingested Antigens.—Constitutional reactions after eating a certain food, inhaling the dander of a certain animal, or excessive exposure to pollen necessitate that the patient carry with him a nebulizer containing epinephrine or a related compound or sublingual isoproterenol (Isuprel) hydrochloride tablets which act within three minutes; antihistaminics or, in the more severe cases, an outfit for injection of epinephrine should be available to him. In my experience even the most severe sensitivity to foods as well as inhalants can be controlled by proper hyposensitization procedures.

Drugs.—Among drugs the most common and most dangerous reactions follow the use of salicylates. It has been stated that patients with nasal polyps are particularly susceptible, perhaps because of their frequent intermittent use of this drug for relief of headaches. A similar situation prevails in asthmatic women with a habit of taking aspirin intermittently at four-week intervals during their menses. Such patients should be alerted to this sensitivity, as their strict avoidance will prevent future trouble. Other analgesics, e. g., acetanilid, or even a mild narcotic, such as codeine, can be substituted for control of pain.

The value of skin testing for drugs is doubtful; conjunctival tests are occasionally of assistance in diagnosing sensitivity to drugs. Tuft's use of the buccal test[9] for determination of drug sensitivity may have merit.

For prevention of allergic reactions from local anesthetics and from sclerosing injections of veins a preliminary small amount should be administered before giving the total dose; 0.05 cc. of a local anesthetic may be injected intradermally into the oral mucosa as a test. If such a small dose elicits a constitutional reaction, it will be less severe than one from a full dose. With orally administered antibiotics a preliminary small oral test dose is recommended prior to administration of the full dose. Patch tests and conjunctival tests may or may not be of value.

2930 W. Grand Blvd. (2).

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THE INCREASING INCIDENCE OF CARCINOMA OF THE THYROID IN A SURGICAL PRACTICE

J. Martin Miller, M.D., Robert C. Horn, M.D.
and
Melvin A. Block, M.D., Detroit

A total of 117 persons with thyroid carcinoma were admitted to a hospital in a period of 15 years. The number from 1943 to 1953 was 34, and the mean annual morbidity for that period was calculated to be between 3 and 4. The mean annual morbidity for thyroid carcinoma in the next five years (1953 to 1957) was between 16 and 17, a marked increase over the previous period. One-fourth of this increased morbidity was accounted for by valid reasons such as the great number of patients seen at the hospital and examined for diseases of the thyroid. Since only a part of the apparent statistical increase in thyroid carcinoma could be accounted for, further investigation is desirable. The possibility that there has been an actual increase in the occurrence of carcinoma of the thyroid could not be ignored.

The value of surgery in the eradication and prophylaxis of thyroid cancer has been under continuous study at the Henry Ford Hospital during the past four years. Beyond these practical aspects, studies have been made of the morbidity and mortality implications of thyroid cancer and yearly statistics have been compiled so that results of current therapeutic principles might be critically inspected. In 1953, the paucity of patients with thyroid cancer in a large medical practice was evident in that 34 cases had been seen in the preceding 10 years, or between 3 and 4 a year. By contrast, 83 cases were seen in the five years from 1953 through 1957, or between 16 and 17 cases per year. Since our surgical approach emphasizes the removal of suspicious nodules rather than indiscriminate removal of all thyroid lesions, it was necessary that this striking increase in incidence be evaluated with considerable care. The volume of medical literature dealing with thyroid cancer led us to believe that such a study would be of general as well as local interest.

Throughout this study, patients with thyroid cancer have been divided into two groups. Group 1 comprises all patients with cancer in whom preoperative cancer suspicion ranged from "none at all" to "a high degree" but in whom a clinical diagnosis was not definite. Group 2 contains those patients in whom metastatic disease was revealed or patients with local findings which left no reasonable doubt as to the correct diagnosis. Comparison of these classifications for the two periods from 1943 to 1952 and from 1953 to 1957 reveals that in the first period, 19 group 1 cancers were found in 438 operations for nontoxic nodular goiter. Fifty-six cancers and 636 operations were parallel figures for the second period. There were 15 group 2 cancers in the first period and 27 in the second.

The factors that we have considered in an attempt to account for these striking figures are as follows: (1) an increase in the number of patients, (2) more thyroidectomies in proportion to the number of clinic visits, (3) the possibility that professional growth might have attracted more referrals, (4) better criteria for pathological diagnosis, (5) improved clinical selection of cases for operation, (6) greater awareness of the possibility of cancer in

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From the Division of Endocrinology, Henry Ford Hospital.

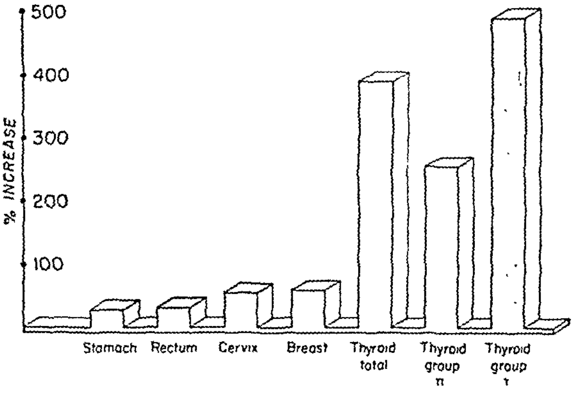
the general population, and (7) the possibility that there has been a real increase in the incidence of thyroid cancer.

Most institutions, medical and otherwise, normally manifest growth with age, and a simple increase in the number of cases of a disease might well be related to this growth. During this second period, 40% more patient visits per year were recorded than for the earlier period. As shown by the figure, four of the more common types of cancer increased in number during this period to a degree anticipated by institutional growth. Cancer of the breast, for example, increased from 45 to 67 cases per year, while cancer of the rectum increased from 35 to 45 cases per year; for both, an average gain of 40%. In sharp contrast is the increase for all thyroid cancer of 390%; group 1, 490%; group 2, 260%.

The growing reputation of an institution for the treatment of one disease or another may result in an increased number of patients referred by family physicians, or of self-referrals when the diagnosis has been established elsewhere. The majority of patients in the present study were self-referred without an established pathological diagnosis. Of the patients with group 1 cancers, three in each period of study were physician-referred, an increase for the second period since it was half as long. Of the patients with group 2 neoplasms, six in the first period and nine in the second were physician-referred or had a previous pathological diagnosis. This represents a greater, though not striking, increase than for the patients with group 1 cancers. These figures statistically are not significantly different but they do indicate that, at best, selective referrals cannot explain more than a small part of the observed increase.

The number of patients with thyroid cancer can be increased in any practice by the simple expedient of increasing the number of thyroidectomies. Judged by Mortensen's statistics from the Mayo Clinic,[1] careful pathological examination of palpably normal thyroid glands should yield two cancers per 100 thyroidectomies, and indiscriminate removal of all glands that are nodular by palpation should raise this number to about four. Our own figures bear this out,[2] and since from 1953 to 1957 the number of thyroidectomies increased from 44 per year to 125 per year, an average of 3 additional cancers each year was assured. With institutional growth accounting for 20% of the increase in the number of operations, these two factors together account for an increase of only about 40% of the increase in patients with group 1 cancers. The number of operations, of course, does not influence the increase in group 2, since these thyroidectomies were performed with a reasonably assured clinical diagnosis of thyroid cancer.

The pathological diagnosis of carcinoma of the thyroid has long been controversial, as witness the eras of "benign metastasizing struma" and "lateral aberrant thyroid." The past decade has seen great improvement in the pathological diagnosis of tumors in general, and outstanding progress has been made in regard to thyroid carcinoma. With this in mind, we have reviewed thyroid tissue from 17 surgically treated patients whose thyroid lesion were originally diagnosed as benign in the 1943 to 1952 era. The same number for the years 1953 to 1955 were re-studied microscopically by one of us (R.C.H.) who has made all the histological diagnoses in 1956 and 1957. Three previously undiagnosed cancers, one of which was occult, were recognized among the 175 cases in the earlier period, and five additional cancers were found in the later group. The number of additional cancers thus found is too small to furnish a basis for accurately estimating the total number of cancers, had all the thyroid cases been reviewed and all material from every case carefully reexamined. It is of interest, nevertheless, to use the results of this review, which represents 45% of the pertinent material, to project hypothetical figures for the corrected total incidence of thyroid cancer for each time period. On this assumption, the corrected total of group 1 cancers would be 26 for 1943 to 1952, and 65 for 1953 to 1957. This still represents a percentage increase of 400, as compared to the 490 derived from the uncorrected figures. Obviously, the improved criteria for pathological diagnoses offer only a partial explanation.



Increased diagnosis of various types of cancer, 1953-1957 over 1943-1952.

In contrast to the above, all diagnoses of thyroid carcinoma between 1943 and 1955 were confirmed on review of the pathological material. Thus, possible differences in pathological interpretation can have no influence on the group 2 statistics. No significant differences were noted in histopathology of the group 1 cancers removed during the two periods (table 1). Whatever its pathogenesis, the increase in thyroid cancer was not selective. A similar pattern of diagnoses for the group 2 cancers has likewise been found for the two time periods (table 2).

Since 1954, patients with nodular goiter have been selected for surgery in a way that would increase the percentage of group 1 cancers; i. e., to recommend operation mainly for those patients in whom something more than the mere presence of a nodule suggested cancer. Three to four per cent seems to be an irreducible minimum, and without selectivity also a maximum. The results of our previously described method of selection[3] are presented in table 3. The number of thyroidectomies per 100,000 professional visits has steadily declined but the number of group 1 cancers has progressively increased. We have already presented a partial explanation of this phenomenon, although it is also possible that a real increase in the incidence of the disease has been a factor.

TABLE 1.—*Pathological Diagnosis of Group 1 Thyroid Cancer*

	1943-1952		1953-1957	
Cell Type	No.	%	No.	%
Papillary	7	37	21	37
Papillary and follicular	1	5	12	21
Follicular	8	42	18	31
Malignant adenoma	2	11	5	9
Undifferentiated	1	5	1	2

In table 4 are shown comparative observations of the two time periods that are of interest. During the second period, 11 times more thyroid nodules, ultimately diagnosed as cancer, were discovered during physical examinations performed for unrelated complaints. Casual observations support the interpretation that better criteria for surgical reference, rather than improved physical diagnosis, were responsible for the improved selectivity. Again, an actual increase in the disease is not ruled out. The size of cancers in group 1 was smaller for the second period, the nodules were apparent for a shorter length of time, and, as in the first period, they were largely asymptomatic. The presence in the series of 10 cancers that were, in essence, accidental findings, raises the possibility that benign nodules are indicators of malignant ones. As noted before, operations on palpably normal glands should yield a pathological diagnosis of cancer of the thyroid in 2%. On this basis, 12 occult cancers would be expected in 636 thyroidectomies and the number of 10 is not unreasonable.

TABLE 2.—*Pathological Diagnosis of Group 2 Thyroid Cancer*

	1943-1952		1953-1957	
Cell Type	No.	%	No.	%
Papillary	6	40	9	33
Papillary and follicular	4	27	6	22
Follicular	2	13	7	26
Malignant adenoma	1	7	0	
Undifferentiated	2	13	4	15
Lymphoma	0		1	4

We note the incidence of cancer in surgical specimens increased from 4 to 15% during the present study. This latter figure parallels those of 10 to 30% usually cited in the surgical literature. That this agreement is brought about by a comparable degree of selection is suggested by a reverse trend reported from the Ochsner Clinic.[4] In their 1942 to 1949 series of patients operated on for solitary thyroid nodules, the incidence of cancer was 19.8%. In a later series from 1949 to 1956 the incidence was 3.9%. This unusual change might be interpreted as follows: In most areas, the surgical enthusiasm generated by the reported high incidence of thyroid cancers in patients with nodular goiter led to a decreased selectivity. The dictum of "remove all nodules" should lead to a cancer incidence of 3 to 4% in operated cases.

TABLE 3.—*Incidence of Group 1 Thyroid Cancer in Patients with Nodular Goiter*

Yr.	Thyroidectomies per 100,000 Professional Visits	Total No. of Thyroidectomies	Total Cancers	%
1943-1952.......	15	438	19	4.3
1953	46	167	6	3.6
1954	34	125	7	5.6
1955	32	131	14	10.6
1956	25	111	15	13.5
1957	22	102	14	13.7

The number of operations for nontoxic nodular goiter almost tripled from one observation period to the next, but the age distribution of the patients so operated remained surprisingly constant. In table 5 the increase appears evenly distributed throughout the age range. The number of cancers discovered, however, increased disproportionately in the younger age groups with only 15% of group 1 cancers being found in patients under 40 years of age for the period 1943 to 1952. A comparative figure of 55% for the later five-year period indicates

TABLE 4.—*Comparative Observations for Group 1 Thyroid Cancer*

	1943-1952		1953-1957	
	No.	%	No.	%
Total no.	19		56	
Discovered on routine physical examination	2	10	22	40
Asymptomatic	13	68	48	84
Over 2 cm. in size	11	58	19	37
Cancer not palpable	1	5	7	12
Small cancer focus in large nodule	3	15	3	5
Lesion present 1 yr. or more	17	90	35	60
Av. age if over 1 yr.	5.5 yr.		3.5 yr.	

either greater medical significance was attached to nodules found during this time or a real increase occurred in the incidence of the disease.

The factor of selectivity, of course, is of no consequence in the increase in number of group 2 cancers. The comparative clinical features do not throw appreciable light on the reasons for the increase in this group (table 6). Although the youth movement evident in the group 1 statistics is not nearly so striking here, nevertheless, only one patient with group 2 cancer was diagnosed under the age of 20 in the early period, while six were seen in the last five years.

Table 5.—*Age Distribution of Patients Operated on for Nodular Goiter and for Group 1 Thyroid Cancers, by Percentage*

Age, Yr.	1943-1952 Thyroidectomies	Group 1 Cancer	1953-1957 Thyroidectomies	Group 1 Cancer
10-19...........	1	15	1	55
20-29...........	8		9	
30-39...........	22		26	
40-49...........	28	85	28	45
50-59...........	30		25	
60-69...........	10		9	
70-79...........	1		1	

Better public education as to the significance of lumps anywhere in the body may have been responsible for increased numbers of self-referrals of patients with cancers that were still 10 years to a lifetime away from clinical significance. This was not evident in breast cancer, however, another lesion presenting as a lump.

In table 7, relative values have been assigned to the various factors possibly significant in the increase of both group 1 and group 2 cancers. The values are obviously approximate and subject to considerable statistical error. The increased number of patients with group 1 cancers can probably be explained without postulating an increase in the incidence of thyroid cancer in the general population. The present study, however, does not completely eliminate this possibility, and we believe that further careful analysis of this aspect is essential. Whether factors other than those of changing institutional practice, public education, and chance account for the increased number of patients with group 2 cancers is more difficult to decide. Here again, definite evidence is lacking, but the figures more strongly suggest a real increase in thyroid cancer. Since the total number is small, a more definite statement is unwarranted. In this age of preventive surgery, it is important not to perform wholesale thyroidectomies because of a statistical increase in the incidence of thyroid cancers. This increase may be more apparent than real and to needlessly raise surgical morbidity would be contrary to medical aims. It is equally important, however, not to blind ourselves to the possibility that a true increase in incidence of thyroid cancer might considerably alter the approach to any program of selection of cases of nodular goiter for surgical treatment.

Table 6.—*Comparative Observations for Group 2 Thyroid Cancer*

	1943-1952		1953-1957	
	No.	%	No.	%
Total no.	15		27	
History of goiter of over 1 yr.	1		5	
Thyroid normal to palpation	7	46	10	38
Palpable regional metastases	11	73	15	58
Distant metastases	3	20	7	23
Under age 40	7	47	12	44
Under age 20	1	7	6	22

Summary

A significant increase has been observed in the incidence of cancer in patients with thyroid malignancy. For the patients with a clinically undiagnosed thyroid cancer, qualitative and quantitative changes in patient population, greater number of operations for nontoxic nodular goiter, and improved clinical selection may account for most of the increase. The increased number of frank thyroid cancers is more difficult to explain on such grounds and suggests that the incidence of thyroid cancer in the general population is increasing. Physicians should regard the approach to preventive surgery of thyroid cancer as being in a dynamic state.

Table 7.—*Summary of Factors Considered Responsible for the Observed Increase in Thyroid Cancer*

	Group 1	Group 2
Institutional growth	8%	15%
Institutional prestige	2%	30%
No. of thyroidectomies	30%	0
Changing pathological criteria	18%	0
Improved clinical selection	20–?	0
Increased self-referral	?	?
Increased incidence in the general population	?	?

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SURVIVAL RATE OF PATIENTS WITH BREAST CANCER IN A SMALL COMMUNITY

Charles P. Barnett, M.D., Fredericksburg, Va.

Halsted's first published report in 1907[1] showed a five-year salvage rate of 28.9% for patients with breast cancer. This has been followed by many other reports, all showing an increasing survival rate. This trend is best shown in results obtained at the Massachusetts General Hospital and the Presbyterian Hospital of New York from 1911 to 1942.[2] The former shows an increase of 27 to 51%, while the latter is almost identical. The current five-year salvage figures for patients with breast cancer from a number of major teaching centers are summarized in table 1.

The wide variation in results may reflect the types of cases included as much as the mode of therapy. Nevertheless, Urban[3] stated that "most American clinics report a five-year salvage rate of about 55% at present" and supported this with a 54% rate for 800 cases from 1945 to 1948.

Whatever the most representative figure may be, it would seem logical for each community or institution to determine its own results in patients with breast cancer. It may be comforting to extrapolate a 55% survival rate to one's own hospital, but it is scarcely realistic. Many hospitals, and even whole communities, can never assemble the formidable numbers of cases that a major institution can in a year or two. Nevertheless, it is not unreasonable for a hospital or medical community to assess the results of its own cases, no matter how few, gathering whatever consolation or remorse the figures may offer when they are compared to established standards.

An attempt was made to collect data on the cases of breast cancer seen by local physicians in this area from July, 1947, through December, 1958. It was hoped this might answer the question "What happens to breast cancer patients in the Fredericksburg area?"

Materials and Methods

The Mary Washington Hospital serves the city of Fredericksburg, Va., and the surrounding area, with a present medical drawing population estimated at 50,000. Most of the surgical procedures were done by three surgeons, all of whom have been certified since the close of World War II. Case data were collected by surveying old operative log books, surgical pathology sheets, and death certificates and by contacts with the local physicians. One hundred three cases of breast cancer are known to have been seen by area physicians in the 11½-year period covered.

The 37% over-all survival rate revealed in this survey of 100 patients offers little evidence that significant progress has been made since the first such study was published by Halsted in 1907. Even when the figures are corrected to produce a 47% rate, there is little reason for complacency. It would seem logical for each community or institution to assess its results, no matter how few the cases, gathering whatever consolation or remorse the figures may offer when they are compared to established standards.

Results

The current status of 100 of the 103 patients has been determined. Assuming the three lost patients to be dead of disease, then 59 patients are determined to have lived five years or more or to have died in less than five years.

Five-year Survival Rates.—The five-year survival rates are shown in table 2. Of the 59 patients 22 lived at least five years, for a 37% over-all survival rate. If the three "lost" cases are not included in the total, the five-year survival rate then becomes 39%. Ten patients were obviously inoperable on the face of the chart and were subjected to biopsy or palliative mastectomy. Four received no surgical treatment. If these 14 cases are excluded, 45 operative cases remain, and 21 patients, or 47%, survived five years. If the three "lost" cases are deleted, the operative five-year rate then becomes 50%. Of 68 patients with known results 41, or 60%, lived three years.

The age distribution, duration of symptoms, and size of lesions are shown in table 3. In 33 cases, or 46%, the axillary nodes showed evidence of metastases. In 42 cases, or 54%, they did not. Radical mastectomy was performed in 74 patients and simple mastectomy in 19. The relationship of axillary metastases to survival is shown in table 4. Of 15 patients undergoing simple mastectomy 4, or 27%, survived 5 years.

Comment

To have meaning any survival figures must be measured against the unmodified course of the disease. Daland's[4] 100 untreated cases are generally accepted as representing the natural history of breast cancer. Shimkin[5] has collected other untreated series of cases and incorporated the results graphically. All show about 20% five-year and 35 to 40% three-year survival rates. If this is accepted as a line of departure then one may conclude that the 37% over-all survival rate in the Fredericksburg

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From the Pathology Laboratory, Mary Washington Hospital.

area represents a favorable influence of treatment. This result differs but little from the 35.5% over-all rate at the University of Pennsylvania[6] and the 39.6% over-all rate from the Memorial Center between 1935 and 1942.[7]

Table 1.—*Representative Five-year Survival Rates for Patients with Breast Cancer*

Location or Institution	Operative Rate	Over-all Rate
Presbyterian Hospital, No. 4 (Haagensen, C. D.: Am. J. Roentgenol. **62**:328, 1949)	47.2	......
Memorial Center for Cancer and Allied Diseases (Adair[7])	54.3	39.6
University of Pennsylvania (Miller and Pendergrass[6])	49.7	35.5
New York state survey (Burdick and Chanatry[12])	43.0	......
Cleveland Clinic (Robnett, A. H., and others: Cancer **3**:757, 1950)	47.7	......
University of Michigan (Bryant and others[10])	58.0	......
Scotland (McWhirter, R.: Brit. J. Radiol. **28**:128, 1955)	58.0	42.0

When only the operable cases are considered the survival rate reaches 47%, slightly more than was found in another small series[8] but less than the 51% obtained in a collection of 49 cases.[9] Various centers report five-year survival rates of 49.7%,[6] 54%,[3] and 58%.[10] The three-year survival rate of 60% is little different from the 62% found at the Memorial Center.[3]

The 62% five-year survival rate of patients reported as having no metastases to the axillary nodes is less than the 75% considered attainable.[11] This suggests that pathological or surgical dissection was inadequate. If the fault were with the former it would have no bearing on the over-all operative results but would only change the grouping. Less than half the cases were reported to show such metastases, quite the reverse of the expectation. This, too, would indicate deficient pathological or surgical dissection. The New York state survey[12] also found an equal distribution of lymph node metastases. Here, also, large numbers of protocols did not comment on the state of the nodes.

Table 2.—*Five-year Survival Rates of Patients with Breast Cancer in Area of Fredericksburg, Va., 1947-1958*

Rate	No. of Cases	Living	Dead	5-Yr. Survival, %
Over-all	59	22	37	37
Corrected over-all	56	22	34	39
Operative	45	21	24	47
Corrected operative	42	21	21	50

The duration of symptoms prior to seeking treatment did not differ significantly from the New York state findings. The size of the lesion is also a crude index of duration, and the distribution of lesions according to size did not vary greatly from the expectation.[13] Both of these factors indicate that patients in this area are not being seen, on the average, much later than elsewhere. Of those surviving five years 80% reported for treatment within a month of discovering the lump, while of those dying in five years only one-third were seen within a month. (Race did not seem to be a factor in seeking treatment; 18% of the patients were Negroes, about the percentage of the Negro population in the area.)

Table 3.—*Age, Duration of Symptoms, and Size of Lesion in Patients with Breast Cancer*

	Cases	
Age, Yr.*	No.	%
20-30	6	6
30-50	40	40
50-70	34	34
over 70	19	19
Duration†		
1 wk.or less	14	17
2 wk.	14	17
1 mo.	17	20
3 mo.	8	9
6 mo.	10	12
1 yr. or more	21	25
Size, Cm.‡		
Less than 1	15	18
1-2	16	20
2-4	29	36
Over 4	20	25

* n = 99
† n = 84
‡ n = 80

The 103 cases are felt to represent nearly all of the breast cancer occurring in the area in the past 11½ years. All patients treated in the hospital and all patients dying in the hospital or in the city limits are included. Death certificates from the counties are not filed locally. However, one county has no physician and patients are treated by Fredericksburg physicians. The other county has two physicians, one of whom has seen no breast cancer in the past 10 years. Conversation with local physicians has revealed only two or three additional cases which, because of lack of information, are not included. No doubt occasional patients may die at home of, or with, untreated breast cancer. Six patients had surgery done elsewhere, but these were all known to, and their progress followed terminally by, local physicians. If the average medical population of the area over the past 11 years is taken at 35,000, then the annual incidence would approximate 28 cases of breast cancer per 100,000 population. This is not far from the 30 per 100,000 population incidence reported in New York state.[14] The collected cases may represent at least 90% of all cases that have occurred in the area.

Table 4.—*Relationship of Axillary Node Metastases and Survival in Thirty-three Patients with Breast Cancer*

		5-Yr. Survival	
Metastases	No. of Cases	No.	%
Yes	17	6	35
No	16	10	62

It would be interesting to know what other small medical communities achieve in the treatment of breast cancer. Certainly the local over-all salvage rate of 37% offers little comfort. Even when the figures are corrected so as to produce a 47% rate of operative salvage there is little cause for complacency, since patients continue to die of the disease after the five-year mark. Perhaps it is wrong to regard Daland's 20% five-year survival rate as the therapeutic base line. Indeed, Collins[15] stated that "approximately 40% of breast cancers either grow locally and can be completely removed or grow so slowly that more than five years are required for recurrences to become manifest."

1410 Royston St.

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CHRONIC THYROIDITIS IN CHILDHOOD

Harmon Brown, M.D.
and
William C. McGarity, M.D., Atlanta, Ga.

Diffuse enlargement of the thyroid gland, low protein-bound iodine value, and the appearance of a nodule in one lobe of the thyroid in an 11-year-old girl led to the diagnosis of thyroid disease with the possibility of carcinoma. At operation the entire gland was found to be diffusely enlarged to about three times normal size. Enough tissue was removed for microscopic study to reveal striking alterations of the follicular architecture. The pathological diagnosis was acute and chronic nonspecific thyroiditis. Records of only 31 comparable cases have been found in a search of the literature. The patient was treated postoperatively with thyroid extract. Six months after operation the patient was receiving a maintenance dosage of 64 mg. of thyroid extract per day; she appeared clinically euthyroid, and the protein-bound iodine value was normal.

Chronic thyroiditis is a relatively rare cause of goiter in children. Only 31 patients with this disorder have been found after a search of the literature. Most of the diagnoses were made after operation for a goiter which was causing pressure symptoms or because carcinoma could not be ruled out in a nodular goiter. In only a few instances was the diagnosis suspected clinically and confirmed by needle biopsy. On the other hand, Winship,[1] in 1956, was able to collect data on 334 patients under 15 years of age with thyroid carcinoma. It is obvious that chronic thyroiditis is a much more unusual cause of goiter in this age group. To re-emphasize thyroiditis, case histories of previously reported patients are reviewed below and the history of an additional patient is presented in detail. With the advent of newer diagnostic techniques, nonoperative diagnosis may be made if thyroiditis is considered.

From the Department of Medicine and the Whitehead Department of Surgery, Emory University School of Medicine.

Report of a Case

An 11-year-old girl was seen in the Emory University Clinic on July 21, 1958. Her illness had begun in December, 1954, when she was noted to have mild exophthalmos. There were no other signs or symptoms of thyrotoxicosis. A basal metabolic rate was -15%. Subsequently, her exophthalmos did not change, and she showed no evidence of thyroid dysfunction. In October, 1957, a diffusely enlarged thyroid gland was noted, and the protein-bound iodine value was 3.8 mcg. %. She appeared to be euthyroid. There were no pressure symptoms. In June, 1958, a nodule was discovered in the left lobe of the thyroid gland. Chest x-ray showed normal results. There was no history of irradiation to the thymus or tonsils.

Physical examination revealed a healthy, well-developed, preadolescent girl. The pulse was 88 per minute and the blood pressure 108/66 mm. Hg. There was slight widening of the palpebral fissures but no exophthalmos. There was no evidence of hyperthyroidism or hypothyroidism. The thyroid gland was three times normal size bilaterally, quite firm, slightly fixed, and nontender. There was an indefinite 1-cm. nodule in the left lower pole, with adjacent enlargement of the isthmus to 1 cm. in diameter. In the right lower pole there was a smaller ill-defined nodule. Two centimeters above and lateral to the left upper pole was a solitary 1-cm., firm, movable, nontender lymph node. The clinical impression was possible thyroid carcinoma.

Laboratory studies showed a hemoglobin level of 12.9 Gm. %. The sedimentation rate was 14 mm. per hour (Westergren); white blood cell count was 5,100 per cubic millimeter, with differential count of 51% segmented neutrophils, 41% lymphocytes, 5% eosinophils, and 3% monocytes. The chest roentgenogram was normal.

The protein-bound iodine value was 3.2 mcg. %. The 24-hour uptake of radioactive iodine (I^{131}) was 8.5%. The scanogram of the thyroid showed most of the I^{131} concentrated in the nodular areas (fig. 1).

On July 30, 1958, an operation was performed. The entire thyroid gland was diffusely enlarged to about three times normal size. The left lower pole and isthmus were larger than the remaining gland. The thyroid gland was firm, and no definite solitary nodules were found. The entire structure had a picture of nodularity. The gland was adherent to the pretracheal muscles and trachea. There was one large pretracheal lymph node, 1 cm. in diameter, superior to the isthmus, and there were numerous enlarged lymph nodes inferior to the isthmus, extending into the superior mediastinum. Several of these lymph nodes were removed and on frozen section revealed hyperplasia with no evidence of malignancy. Since the predominant disease was located in the left lower pole and the isthmus, this portion of the thyroid gland was removed and submitted for pathological studies. A definite diagnosis of a malignancy or a benign process could not be determined from frozen section studies, so it was decided to discontinue surgery at this point until permanent sections were completed. Because of the patient's age and possibility of thyroiditis and future development of hypothyroidism, it was felt desirable to remove only enough tissue at this time to establish a diagnosis.

The pathological description was supplied by the department of pathology, Emory University Hospital. The specimen consisted of thyroid tissue weighing 4 Gm. and measuring 2.2 by 1.5 by 0.5 cm. The external surface was irregular and transmitted a grayish-red color with moderately accentuated vascularity. The consistency of the tissue did not appear remarkable, although there was a suggestion of nodularity. On cut surface the tissue had a yellowish-pink color and appeared divided into many small lobulations 2 to 3 mm. in diameter. Separately submitted were six lymph nodes measuring up to 0.5 cm. in diameter. These were unremarkable in consistency and had a homogeneous glistening grayish-yellow cut surface. On microscopic examination the architectural pattern of the thyroid tissue was markedly distorted (fig. 2).

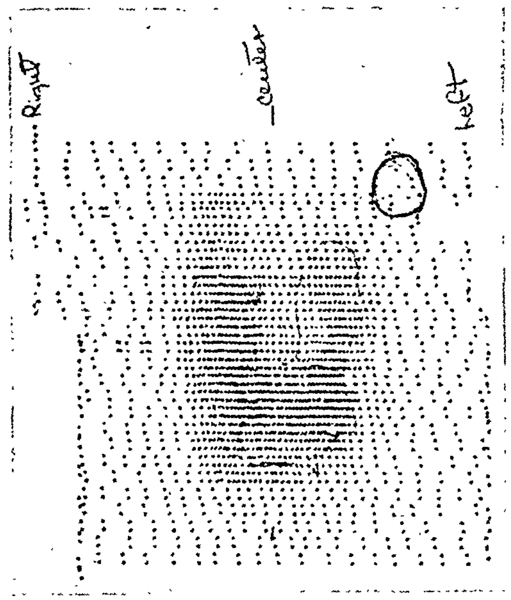

Fig. 1.—Radioactive iodine concentrated in lower left pole and isthmus. Enlarged cervical lymph node is circled at upper right.

There was a distinct nodular pattern, the nodules being separated by thin bands of connective tissue. Within each nodule considerable variation in pattern was observable. The most striking alteration was that of the follicular architecture, which in many areas took on a distinctly papillary configuration and in other areas appeared to form large anastomosing channels. In most areas the epithelium was tall cuboidal or columnar, and small amounts of colloid were present. In other areas there was cystic dilatation of follicles with a flat epithelium and the accumulation of large amounts of thin staining colloid. In a few areas the thyroid tissue appeared to have undergone considerable atrophy and replacement by fibrous tissue. In most of the nodules there was striking interstitial infiltration of lymphocytes, plasma cells, and mononuclear phagocytes, and in several areas distinct lymphoid follicles were seen. Despite the marked variation in the appearance of the follicular epithelium and its tendency to a papillary configuration, the follicular cells appeared remarkably uniform in all areas and showed very little evidence of proliferative activity. The separately submitted lymph nodes showed some hyperplasia of the lymphoid follicles and a moderate degree of subacute and chronic lymphadenitis. The pathological diagnosis was subacute and chronic nonspecific thyroiditis.

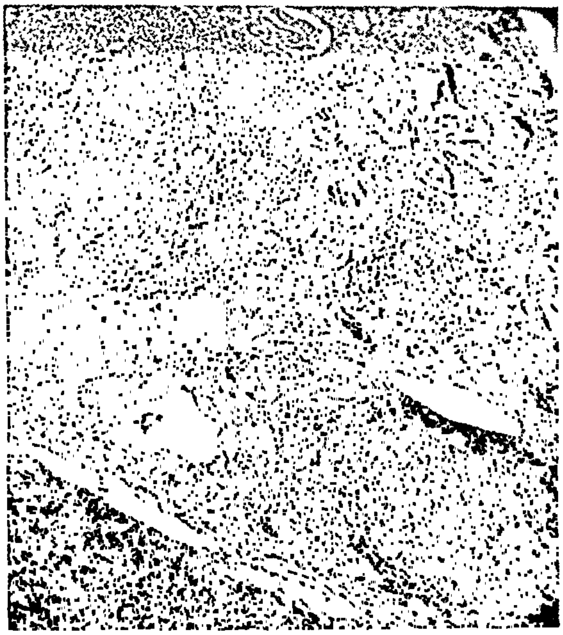

Fig. 2.—Section showing dilated follicle with flat epithelium and infiltration with lymphocytes and mononuclear phagocytes forming lymphoid follicles.

The immediate postoperative course was uneventful. The patient was seen four weeks after operation. The operative site was well-healed, and the remaining thyroid tissue was unchanged. The deep tendon reflexes showed slight prolongation of the relaxation phase. Therapy with thyroid extract, 32 mg. daily, was begun. This was increased to 64 mg. daily in a few weeks. Six months after surgery the patient was clinically euthyroid and the residual thyroid tissue was unchanged. The protein-bound iodine value at this time was 6.4 mcg. %.

Comment

It is difficult to determine the relative occurrence of this lesion in children, as there are so few reports. Pemberton and Black[2] reviewed the cases of 52 children, 14 years old and under, who were operated on for nontoxic nodular goiter at the Mayo Clinic from 1908 through 1943. They found only two patients with thyroiditis. Of the remaining 50, 32 had adenoma and 18 carcinoma. Norris and Pollock[3] reported their experience over an 18-year period at Los Angeles Children's Hospital. Of 14 children operated on for nontoxic goiter, 2 girls, aged 7 and 10, had typical struma lymphomatosa (Hashimoto's struma), 9 had adenomas, and 3 had malignancy.

Crawford[4] states that one-half of the patients with nontoxic goiters seen in the Pediatric Endocrine Clinic at Massachusetts General Hospital have either adolescent goiters or chronic lymphocytic thyroiditis (Hashimoto's disease). These patients are nearly all female, from ages 9 through adolescence. Thus, it would seem that thyroiditis is not uncommon in the experience of this clinic. On the other hand, Buxton[5] described only 2 patients among 173 with nontoxic goiters studied at the University of Michigan and the University of Maryland. In one the gland was diffusely enlarged, and in the other it was a solitary nodule. Only 18 patients in this group had nodular goiters.

Since the classic description of the two major types of chronic thyroiditis by Riedel and Hashimoto, much interest has been shown in this group of diseases. Excellent reviews[6] of the subject have been written but are beyond the scope of this discussion.

In 1938, the first reports of struma lymphomatosa occurring in childhood were made by Hellwig[7] and others. Joll,[6b] in his excellent Hunterian lecture in 1939, mentioned a 10-year-old girl. Only isolated reports were made until Statland's[6c] summarized 51 cases of struma lymphomatosa from Massachusetts General Hospital, in which three young girls were studied.

The most complete study of this disorder in children is that of Gribetz and others.[8] They described six adolescent and preadolescent girls with firm goiters which were two to four times normal size and granular or nodular. The Delphian node or pyramidal lobe was enlarged in all instances.

Our patient exhibited several features of this disorder in common with features of others already reported in the literature. A long history of goiter was frequently reported. Enlargement of the thyroid had been present for an average of four years, ranging from seven months to eight years. In a few there was slow progression of the goiter, with a sudden increase in growth rate in the months before definitive therapy was started. The average age at which a goiter was first noted was 9 years (in 15 patients). The majority of the patients, 27 of 31, were female. On examination, the thyroid was generally quite firm, three to four times normal size, with nodularity or lobulation by palpation. These characteristics have been described in 20 of the 31 patients previously reported. Although thyroiditis is a diffuse process, the surface of the gland tends to be irregular or nodular. In only one instance has the thyroid been reported as being diffusely enlarged with a smooth surface. Two patients presented clinically as having only a solitary nodule.

Because of the firm consistency, nodularity, and the frequent occurrence of cervical adenopathy, the diagnosis of carcinoma is often considered. However, thyroiditis is a diffuse process and usually causes enlargement of the entire gland. On the other hand, patients with early carcinoma usually have a solitary nodule or enlargement of a portion of the gland.

The symptoms are related to the local effects of a goiter. These are a sense of fulness or pressure, mild dysphagia, or hoarseness. Most of the patients are clinically euthyroid or only mildly hypothyroid. In only one instance has severe myxedema been present.[8] However, surgical procedures hasten the onset of hypothyroidism, probably in two ways: (1) by removal of functioning tissue and (2) by further release of antithyroid antibodies.

As yet, there is no laboratory test which may be considered specific, but several of the routine tests of thyroid function may be suggestive, if used in combination. The radioactive iodine uptake and serum cholesterol level are usually within normal limits. The basal metabolic rate is usually low-normal or low. In five cases where this test was done, values have ranged from −6 to −25%. However, the finding of a low basal metabolic rate and an elevated I^{131} uptake is quite suggestive.

Gribetz and others[8] and Skillern and others[6d] have noted an abnormal discrepancy between protein-bound iodine and butanol-extractable iodine values. In several patients the protein-bound iodine value was elevated while the butanol-extractable iodine value was normal or low. They felt that this was due to a disorder of synthesis and release of thyroid hormone, liberating calorigenically inactive substances into the blood stream. This situation was reversed in all patients by the administration of thyroid hormone, which also caused a decrease in the size of the goiter in most.

Although the radioactive iodine uptake alone is not helpful, failure to increase it after administration of thyrotropin is suggestive of thyroiditis, according to the studies of Skillern and others.[6d] This would indicate that the failing gland is already under maximal stimulation by thyrotropin. Also, the histological changes noted in the acinar epithelium of eosinophilia and high cuboidal structure are those associated with stimulation by the thyrotropic hormone. Thus, it might be expected that the areas most involved might concentrate more radioactive material. In our patient the scanogram showed this to be true. Since toxic nodular goiter has not been reported in children, a differential study in children with nodular goiter may be worthwhile. Most malignant nodules concentrate less iodine than the surrounding thyroid tissue.

The "era of immunology" in thyroiditis began in 1954 with the report, by Cooke and Wilder,[9] of an abnormal serum colloidal gold curve in two patients with struma lymphomatosa. Skillern and associates[6d] demonstrated abnormal colloidal gold curves in 20 of 25 patients. They showed that this finding was due to abnormal distribution of plasma proteins—low or low-normal albumin levels, elevated gamma globulin levels, and low or low-normal alpha globulin levels. They theorized that these findings were due to primary failure of the thyroid gland with thyroxin deficiency, because the gamma globulin level is low in toxic diffuse goiter (Graves' disease) and the abnormalities in plasma protein values and colloidal gold flocculation were corrected by the administration of thyroxin or thyroid extract. They also found abnormalities in other flocculation tests which are related to elevated gamma globulin—thymol turbidity, zinc sulfate turbidity, and cephalin-cholesterol flocculation.

In a series of excellent experiments, Witebsky[10] and associates made several valuable discoveries concerning the organ specificity of extracts of thyroid glands in a variety of animals. 1. Thyroid extracts act as antigens which are capable of eliciting organ-specific antibodies against the thyroid gland. 2. Rabbits injected with extracts of their own thyroid gland produce true autoantibodies. 3. Microscopic changes in the glands of the animals in which antibodies are produced are similar to those seen in chronic thyroiditis.

Roitt and associates[11] have demonstrated precipitin antibodies against extracts of human thyroid gland in a large percentage of patients with chronic lymphocytic thyroiditis (Hashimoto's disease). They have also shown that the active antigen is probably thyroglobulin. Paine and others,[10c] on the other hand, were unable to find antibodies in 14 patients with a surgical or needle biopsy diagnosis of chronic lymphocytic thyroiditis. However, they did find elevated antibody titers in 14 of 18 patients with a histological diagnosis of chronic nonspecific thyroiditis.

If the gland is diffusely enlarged, needle biopsy is a good diagnostic technique. In the presence of a solitary nodule, it is unwise to rely on needle biopsy, as the changes of chronic thyroiditis may be found adjacent to carcinoma. Nearly all solitary nodules should be surgically excised for study. If there is still doubt after all studies have been performed, then surgical biopsy should be done to establish a definite diagnosis.

Treatment

After the diagnosis of chronic thyroiditis is established, therapy with thyroid extract should be started, whether the patient is hypothyroid or euthyroid. This will suppress thyrotropin activity if used in adequate dosage, usually 60 mg. to 240 mg. daily.[6d]

The administration of thyroid extract in most patients with thyroiditis will cause a reduction in size of the goiter within three to six months. If there is a wide difference in protein-bound iodine and butanol-extractable iodine values, this will also be corrected.

If the thyroid is surgically explored, only a minimal amount of tissue should be removed for diagnosis. The isthmus may be removed to prevent pressure symptoms. The patient should then be placed on therapy with thyroid extract, as surgery seems to hasten the onset of hypothyroidism.

Thyroid extract should probably be continued indefinitely, for two reasons—first, to reduce the size of the goiter and prevent its recurrence and, second, to prevent the insidious onset of hypothyroidism in the adolescent. The only satisfactory way to determine the proper dosage level is by periodic determination of the serum protein-bound iodine level or butanol-extractable iodine level while the patient is on therapy with thyroid extract.[12]

Surgery may be necessary later for cosmetic reasons or to relieve obstructive symptoms, if thyroid therapy is ineffective. However, surgery should be delayed if at all possible, since thyroid extract therapy may require as long as a year to achieve reduction in the size of the goiter. Usually, maximal effect is achieved in three to six months.

Summary

Chronic thyroiditis is unusual in childhood and early adolescence. Only 31 cases have been found in the literature. There are usually no symptoms except for the presence of a goiter, but pressure symptoms may occur. If hypothyroidism develops, it does so late in the course of the disease. The gland is usually three to four times larger than normal, is firm, and may feel lobular or nodular. Most of the patients are female.

The diagnosis of chronic thyroiditis may be suspected on many clinical and laboratory bases: (1) a young female with a firm, nodular goiter and the findings of hypothyroidism; (2) an elevated protein-bound iodine level and relatively low butanol-extractable iodine level; (3) evidence of increased serum gamma globulin by serum electrophoresis and elevated serum colloidal gold flocculation, thymol turbidity, or zinc sulfate turbidity; and (4) the demonstration of specific antithyroid antibodies in the serum.

Needle biopsy or surgery may be necessary to establish a definite diagnosis. Once diagnosis has been made, the patient should be treated with thyroid extract in adequate dosage to maintain the protein-bound iodine level or butanol-extractable iodine level within normal range. Surgery may be necessary if an adequate trial of thyroid extract therapy proves ineffective in reducing the size of the gland and if pressure symptoms develop.

The histological description given for the patient in this study was made by Dr. Abner Golden, Department of Pathology, Emory University Hospital and Emory University School of Medicine.

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ESOPHAGEAL REPLACEMENT IN INFANTS AND CHILDREN WITH USE OF A SEGMENT OF COLON

Luther A. Longino, M.D., Morton M. Woolley, M.D.
and
Robert E. Gross, M.D., Boston

A segment of colon is considered best for operative substitution of a damaged esophagus because it resists peptic ulceration, it functions well during swallowing, and its blood supply remains intact after transposition. Before a child is considered a candidate for the operation, conservative treatment should be done (dilatation for esophageal stricture, portal-systemic venous anastomosis for varices). The operation was performed successfully on six of nine infants with congenital esophageal atresia, four children with strictures from ingested lye, two with persistent esophagitis, and three with bleeding varices. Failure of the operative procedure was the cause of death in one child; in the others the cause was undetermined or unrelated. The technical difficulties of the transposition are encountered in the infant, and these can usually be obviated by delaying the operation until the child is 1 to 2 years old.

There are numerous disease processes involving the esophagus which require partial or total esophageal replacement. In the pediatric age group esophageal replacement is done for one, or a combination, of the following reasons: (1) esophageal atresia without adequate esophageal substance for primary anastomosis, (2) caustic strictures, (3) peptic esophagitis with stricture formation or bleeding, and (4) bleeding varices when portal-systemic shunts have failed to control bleeding.

In the Boston Children's Hospital we have had experience with these four esophageal lesions, and there is good reason to believe that we will see an increasing number of children with bleeding varices who will need esophageal resection and replacement therapy.

A satisfactory substitute for the esophagus should meet the following specifications: 1. It must serve as a satisfactory conduit for food and fluids to reach the stomach so that the patient can maintain satisfactory nutrition without taking prolonged periods of time for each feeding or meal. 2. The conduit must be anatomically small enough so that pulmonary function is not interfered with during a feeding. 3. The substitute must be sufficiently resistant to peptic juices so that ulceration, stricture, or bleeding are not frequent complications. 4. Formation of the substitute esophagus must be technically feasible for replacement of part or all of the esophagus with adequate blood supply for both proximal and distal anastomoses. 5. Preferably, there should be no unsightly cosmetic deformity such as is encountered with a subcutaneous antethoracic type conduit.

In the early years of treatment of esophageal atresia, the formation of a subcutaneous conduit containing small intestine distally and a skin tube proximally was utilized in the salvage of these infants.[1] Antethoracic tubes of small intestine have also been used for caustic strictures.[2] Some of these procedures required multiple major operations and long periods of hospitalization. Anastomotic strictures were frequent complications, and the subcutaneous bulging of the anterior chest wall was cosmetically unsatisfactory.[3] Fistula formation, due to difficulty in maintaining the blood supply in the small intestine, which has rather short arcades, was not uncommon.

Plastic tubes have been used in the replacement of small segments of esophagus when carcinoma has been resected. These cannot be utilized for long segments, and there is a tendency for these tubes to leak at their anastomotic sites.[4]

The thoracic part of the stomach manifests well-known sequelae of peptic esophagitis and dyspepsia which are unpleasant and detrimental to the health of the patient.[5] In 1953 and 1954 we treated four patients with esophageal atresia who had inadequate esophageal length for primary anastomosis. These patients had the stomach mobilized and pulled into the chest for anastomosis to the short proximal esophageal segment. Three of these four patients died in the immediate postoperative period due to atelectasis or aspiration of vomitus. We consider this to be an unsatisfactory type of esophageal replacement because of both the high immediate mortality and the serious late sequelae.

Recently there has been a report of the formation of a tube from the greater curvature of the stomach, this being anastomosed to the esophagus via the suprasternal notch. We have had no experience with this but will be interested in the eventual results of such a procedure.

From the Surgical Service of the Children's Hospital and the Department of Surgery of the Harvard Medical School.

Read before the Section on Surgery, General and Abdominal, at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

At the present time we, along with others, have found the colon to be the most satisfactory replacement for the esophagus.[6] It is resistant to peptic ulceration, and it has a good blood supply which is anatomically arranged so that the marginal artery of Drummond can be utilized to supply a long segment of colon to replace the entire esophagus if this is necessary. Although the colon does not have purposeful propulsive peristalsis, most patients have no difficulty in eating fairly rapidly as long as they eat in an upright position. Since 1953 we have had the opportunity of treating 18 patients (see table) with colon replacement of part or all of the thoracic esophagus. This paper is a report of our experience with these cases, description of the technical aspects of the operation, present status of the procedure, and recommendations.

Indications for and Results of Coloesophagoplasty in Eighteen Patients

Indication	Living, No	Dead, No	Total
Esophageal atresia	6	3	9
Lye stricture	4	0	4
Peptic esophagitis	2	0	2
Bleeding esophageal varices	3	0	3
Total	15	3	18

Esophageal Atresia

The largest group of patients was those with esophageal atresia who had inadequate esophageal length for primary esophageal anastomosis. Nine patients with this anomaly have been treated by colon substitution. These patients usually do not have a tracheoesophageal fistula, so the primary procedure is that of exteriorization of the upper esophageal pouch so that saliva can drain out onto a dressing on the neck rather than constantly spilling over into the trachea, with resultant pneumonitis. A gastrostomy is then performed for feeding purposes until the esophageal replacement can be performed. Occasionally, in the patient with esophageal atresia and tracheoesophageal fistula the esophageal segments will be of inadequate length for primary anastomosis; then the tracheoesophageal fistula must be divided so that reflux of gastric juice into the trachea is prevented. When we first began using the colon as a substitute esophagus, the procedure was performed in the early weeks or months of life. Technical difficulties ensued which have led us to abandon this; we now wait until the child is approximately 20 lb. (9.1 kg.) in weight or 1½ years of age before we attempt the definitive procedure. The following is a typical case presentation.

Case 1.—This 3-day-old infant was admitted to the Boston Children's Hospital on Feb. 18, 1957, weighing 3 lb. 9 oz. (1,587 Gm.). Prior to admission it was noted that he regurgitated feedings through his nose. Subsequent roentgenograms revealed an esophageal atresia without tracheoesophageal fistula. Soon after the patient's admission, the upper esophageal segment was exteriorized in the neck and a Stamm gastrostomy was performed; both procedures were done with the patient under anesthesia with locally given procaine hydrochloride. On March 26, 1957, at the age of 6 weeks, the child weighed 5 lb. 15 oz. (2,693 Gm.) and was discharged from the hospital. The baby was fed by gastrostomy at home and was readmitted to the hospital on June 17, 1958, at the age of 16 months, weighing 24.5 lb. (11.1 kg.). After a succinylsulfathiazole (Sulfasuxidine)–neomycin sulfate preparation and cleansing enemas were given, the child underwent esophageal substitution with use of the ascending colon. Postoperatively, small amounts of saliva leaked through the cervical wound for two weeks and then stopped spontaneously. A roentgenographic study of the esophageal replacement made with barium revealed good function (fig. 1). The child ate well and gained weight.

It should be noticed that this child entered the hospital weighing 3 lb. 9 oz. The prognosis of premature infants with esophageal atresia is improved by minimal procedures necessary to protect the lungs and to allow alimentation. Any definitive procedure should be delayed until the child is gaining weight and is of adequate size to obviate technical difficulties inherent in the small patient. We now consider approximately 1½ years the ideal age for the definitive procedure in these infants.

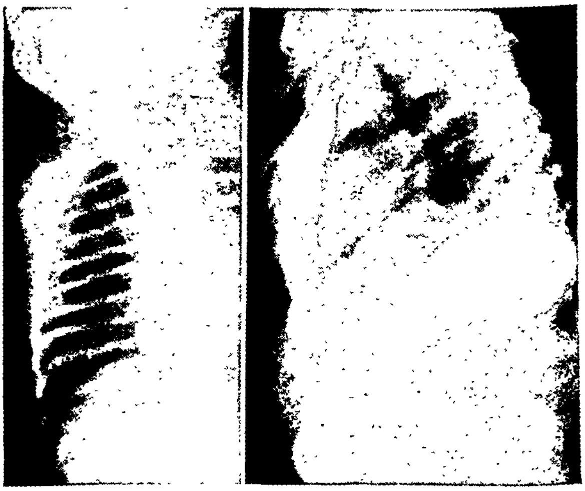

Fig. 1 (case 1).—*Left*, esophageal atresia without fistula. *Right*, retrosternal replacement of the esophagus with use of ascending and transverse colon.

Esophageal Stricture Secondary to Lye Ingestion

We have had four cases of caustic esophageal stricture which have been resistant to dilational therapy. The number of dilations in the four cases have varied between 23 and 100. Exactly how many dilations should be done prior to the recommendation of colon substitution is a matter of individual concern, and more emphasis should be placed on the frequency of necessary dilations rather than the actual number of dilations. The degree of nutritional impairment is also a factor in this decision. The following case is an example of this type therapy in a patient who was resistant to dilational therapy because of extensive and severe stricturing.

Case 2.—At the age of 2 years this child ingested lye. The patient had had two esophageal dilations prior to her admission to the Children's Medical Center six weeks after the lye ingestion. Esophageal dilation was impossible at that time due to the severity of the stricture; therefore, a gastrostomy was performed and a string was passed through the esophagus to facilitate retrograde dilations, with use of Tucker type dilators. During the ensuing 18 months, the child had 23 such dilations, and roentgenograms of the esophagus revealed involvement of practically its entire length. At this time it was felt that further dilations would not be effective except as a temporizing measure; therefore, on May 15, 1958, when the child was aged 4 years and 7 months, the esophageal stricture was bypassed with use of the right part of the transverse colon. A Heineke-Mikulicz pyloroplasty was performed at the same operation. Postoperatively, the child was able to swallow well; therefore the gastrostomy was closed two months later (fig. 2).

Peptic Esophagitis

The majority of infants who have repeated episodes of regurgitation of fluids into the esophagus recover from this abnormal physiological state spontaneously, provided they do not have central nervous system disease. The upright position seems to hasten recovery from this abnormality. Rarely these children do not improve, and some develop severe peptic esophagitis with ensuing stricture formation. We have had two such patients who have required resectional therapy; one of the cases is reported.

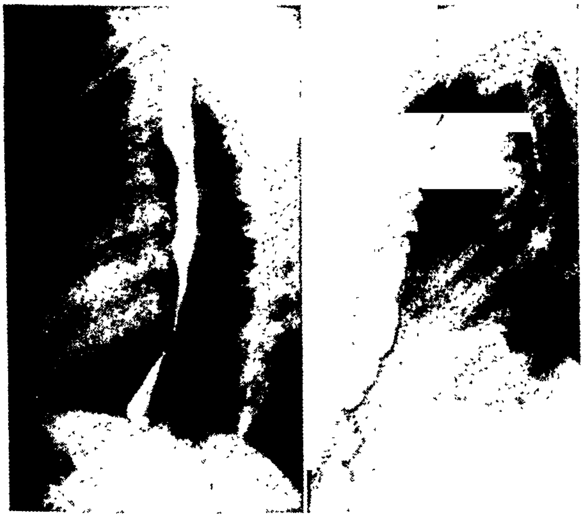
Fig. 2 (case 2).—*Left,* stricture of esophagus, resulting from ingestion of lye, after multiple dilations. *Right,* appearance after colon substitution.

Case 3.—This patient was first seen at the Children's Hospital in June, 1948, at the age of 4½ months because of recurrent vomiting and failure to gain weight. Esophagoscopy revealed severe esophagitis in the lower esophagus. The child was placed on an antacid regimen and was fed in the upright position; however, this regimen was not strictly adhered to at home. She was lost to follow-up and returned at 8 years of age with a very tight stricture of the lower third of the esophagus, which was quite difficult to dilate. She was anemic, and weighed only 36 lb. (16.3 kg.). Between June, 1956, and November, 1957, the child required six esophageal dilations, during which time she gained 16 lb. (7.2 kg.) but could still eat only puréed or very soft foods. On Jan. 9, 1958, she had resection of the lower one-third of her esophagus with interposition of the transverse colon between the proximal esophagus and stomach. This was performed through a left thoracoabdominal incision, and a new esophageal hiatus was formed through the left side of the diaphragm. Four months later the child required one dilation of the anastomosis; since that time she has been able to eat a regular diet without difficulty and is entirely asymptomatic (fig. 3). This syndrome is not common in the pediatric age group; however, when present, it causes severe nutritional inadequacies because of both dysphagia and blood loss.

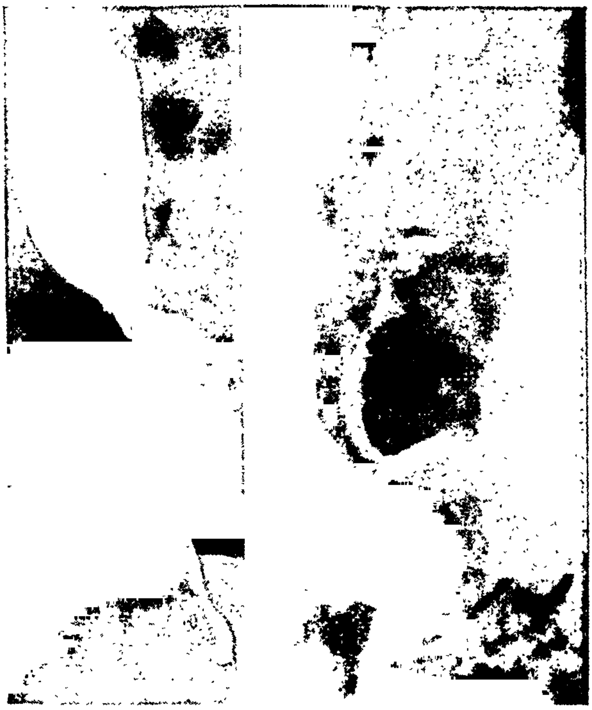
Fig. 3 (case 3).—*Left,* severe peptic esophagitis with stricturing. *Right,* partial esophageal replacement with colon.

Bleeding from Esophageal Varices

The preferable therapy for the patient with bleeding esophageal varices is some type of portal-systemic venous anastomosis. Since the majority of children with bleeding varices have portal vein thrombosis, splenorenal shunt is most commonly employed. If the child has had a previous splenectomy or if the shunt has thrombosed, then one is left only with a direct approach to the bleeding varices. This involves either suturing of the varices or resectional therapy of the affected esophagus and stomach. The following case presentation is of a child who had a splenectomy for congenital spherocytosis followed by bleeding varices. This then required direct attention to the varices.

Case 4.—The patient was first seen in the Children's Hospital on Oct. 21, 1948, at the age of 12 days because of omphalitis. This was treated with antibiotics. The child improved and was discharged. At the age of 4 years he had a splenectomy for congenital spherocytosis. In October, 1956, at the age of 8 years, he vomited blood and was found to have esophageal varices. On Oct. 29, 1956, the esophageal varices were ligated with catgut and silk. During the ensuing two years, he had three minor hemorrhages; then on Dec. 25, 1958, he had an exsanguinating hemorrhage requiring multiple transfusions and esophageal tamponade. The child came close to death during this episode. On Dec. 29, 1958, he underwent resection of the distal third of the esophagus with replacement by transverse colon and pyloroplasty. Postoperatively, the pyloric canal was obstructed and required an anterior gastrojejunostomy. After this the child was able to eat a normal diet. He had no further episodes of bleeding (fig. 4).

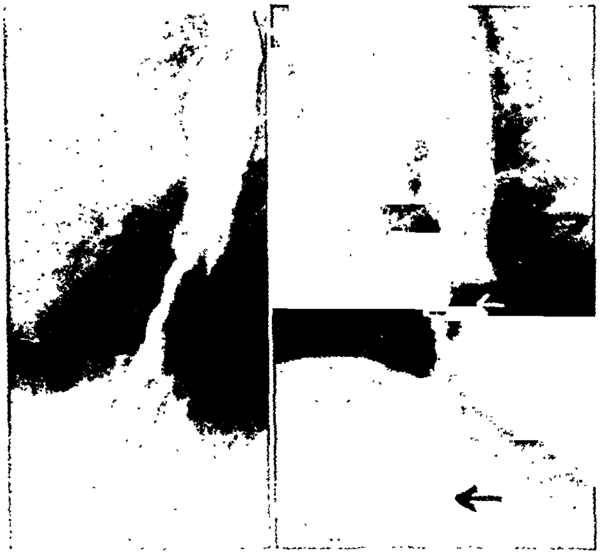

Fig. 4 (case 4).—*Left,* esophageal varices in patient who had previous splenectomy and ligation of esophageal varices with persistent bleeding. *Right,* colon interposition after resection of lower one-third of esophagus and upper one-third of stomach. Interposed section of colon is outlined between arrows.

In a patient who has no available veins in the portal system for shunting, resectional therapy offers the best chance of preventing recurrent life-endangering hemorrhage. Our experience with ligation of varices has been good only as a temporizing measure.

Technique

The technical approach to coloesophagoplasty depends on the amount of esophagus to be replaced or bypassed. The technical aspects of total thoracic coloesophagoplasty as it is now performed routinely in the Boston Children's Hospital will be described first. The patient is placed on the operating table in the supine position, with the hea and neck extended. Preparation and draping include the entire abdomen as well as the chest an neck. The abdominal cavity is entered through a upper right paramedian incision. The omentum i removed from the transverse colon. The entir ascending colon, terminal ileum, hepatic flexure and transverse colon are mobilized. The blood supply to the colon is visualized and careful attentio given to the distribution of the midcolic vessel Bulldog clamps are placed on the ileocolic an right colic vessels so that the colon can be observe for adequate blood supply from the midcolic vessels. The terminal ileum is divided as is the le transverse colon distal to the midcolic arcades. Th actual cautery is used for dividing the intestin and continuity is reestablished by a closed-typ aseptic anastomosis with one layer of interrupte Halsted sutures of 0000 silk. If the blood supply i adequate, the right colic and ileocolic vessels ar divided close to their origin and the ascendin colon is passed behind the stomach, through th hepatogastric ligament, and through a tunnel whic has been formed by blunt dissection behind th sternum.

While this is being done, another operating tea has made a transverse incision low in the nec and dissected between the sternocleidomastoideu muscles, behind the trachea, and isolated the uppe esophagus. The tunnel is then continued fro above, and the terminal part of the ileum and th ascending colon are pulled through this tunnel an out of the cervical incision. A two-layer anastomosis is performed in the neck between the uppe esophageal segment and the colon after the exces ileum, appendix, cecum, and redundant ascendin colon have been removed. Two layers of interrupte 0000 silk are used. This wound is then closed, an a drain is left near the anastomotic site in case o leakage.

The cologastrostomy is then performed with us of an open-type anastomosis with 000 runnin chromic catgut inside and interrupted 0000 sil outside. This is best performed on the lesser curva ture of the stomach; it is not necessary to perform this anastomosis high, because this tends to kink the colon. A Heineke-Mikulicz pyloroplasty is then done to facilitate gastric emptying and to minimize reflux of gastric contents into the colon. A Stamm gastrostomy is done routinely for intestinal decompression and for feeding purposes during the immediate postoperative period. On previous occasions the colon has been passed through a new hiatus in the left leaf of the diaphragm and behind the left lung root, but at present we feel that the retrosternal position has the advantage of not entering the pleural cavity and also of giving a more direct route for the conduit (fig. 5).

If only the lower third of the esophagus is to be replaced, the following procedure is used. The patient is placed on the table in an oblique fashion so that the left anterior part of the chest and left side of the abdomen are uppermost. A thoraco-abdominal incision is used through the seventh or

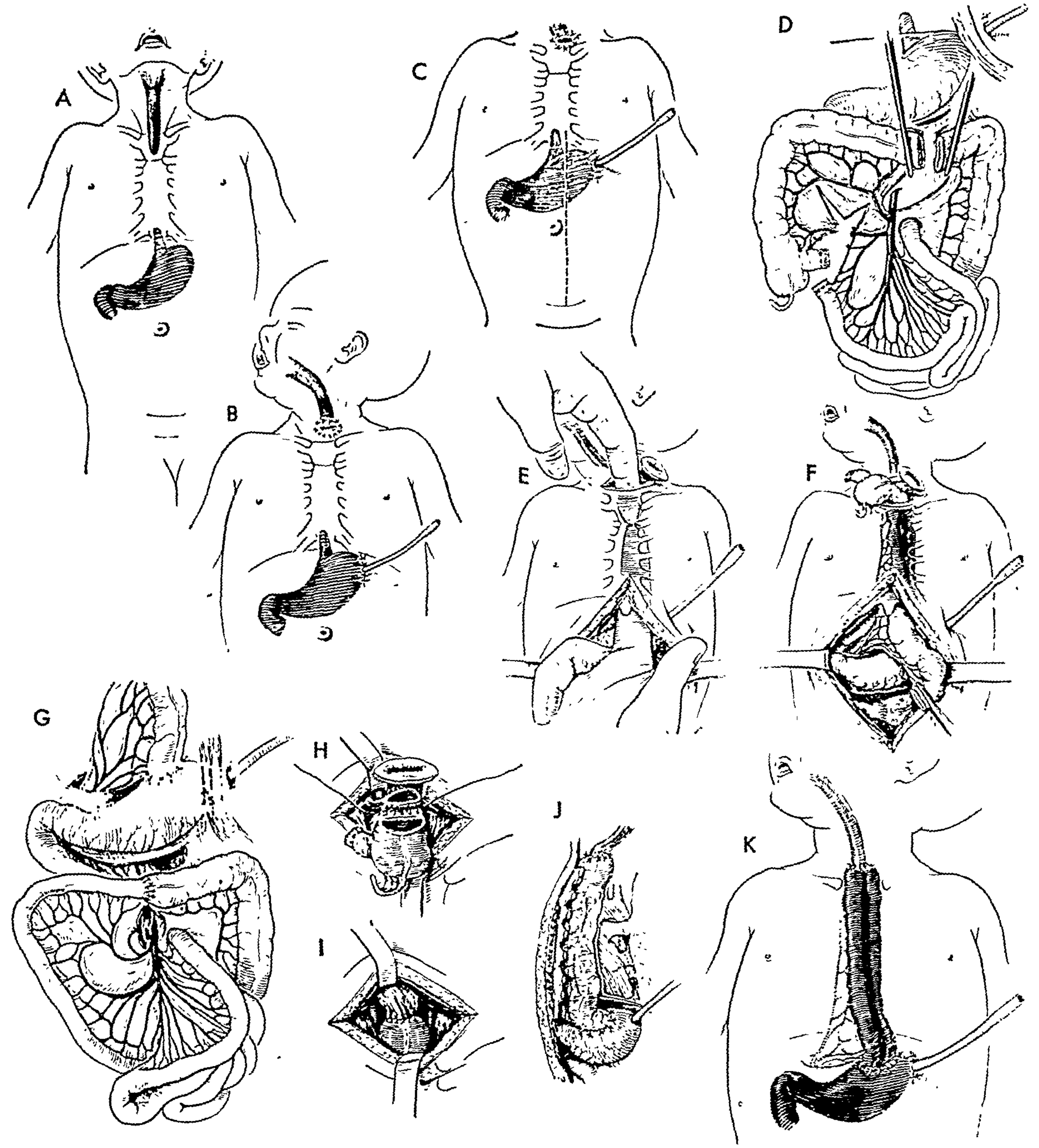

Fig. 5.—*A*, sketch of esophageal atresia at birth and, *B*, after marsupialization of esophagus and gastrostomy; *C*, outline of incision; *D*, mobilization and isolation of colonic segment; *E*, creation of retrosternal tunnel; *F*, mobilized colon within tunnel; *G*, reconstruction of intestinal continuity; *H and I*, details of esophagocolonic anastomosis; *J and K*, position of colon behind sternum with gastrostomy in place for decompression of intestinal tract.

eighth intercostal space. The inferior pulmonary ligament is divided, and as much of the esophagus as is necessary is dissected free for resection. The transverse colon is then freed of its omentum, and a segment of sufficient length is isolated with the midcolic vessels used for blood supply. Actual cautery is used for transecting the intestinal segment, and continuity is reestablished, with use of a closed-type aseptic anastomosis of Halsted sutures of 0000 silk. Either a new hiatus is formed through the left side of the diaphragm or the esophageal hiatus can be utilized in passing the colonic segment into the chest for anastomosis to the esophagus. Two layers of interrupted 0000 silk are used in the upper anastomosis and an inner layer of running 000 chromic catgut and an outer layer of interrupted 0000 silk in the lower anastomosis. Routinely, a Heineke-Mikulicz pyloroplasty is performed. A Stamm gastrostomy is used for intestinal tract decompression as well as for feeding purposes, until the child is ready to swallow.

Results

Nine patients with esophageal atresia have been treated by use of the colon as an esophageal substitute. Six of these children are alive and well at the present time. One patient died one week postoperatively due to necrosis of the colon with anastomotic leaks both proximally and distally. This child also had the gastrostomy tube removed and replaced early in the postoperative period, resulting in dehiscence of the stomach from the anterior abdominal wall; feedings therefore were given in the peritoneal cavity. This child was aged 3 months at the time the coloesophagoplasty was performed. The second fatality was that of a patient who was operated on at 12 days of age and died at home 10 months later. The death was sudden, and unfortunately no autopsy could be performed. The cause of death in this child remains unknown. The third fatality was the result of perforation of the colon, six months after the operative procedure, during attempted dilation. The child died of sepsis secondary to a leak into the left side of the chest. Another child who was operated on a the age of 2 months required revision of both anastomoses due to stricturing and torsion of the colon. In the recent cases these technical difficulties have been obviated by waiting until the child has become older and larger. We think that this will decrease our number of complications as well as fatalities.

Four patients with stricture of the esophagus due to ingestion of lye, who have been resistant to dilational therapy, have been operated on. One patient developed a small-intestinal obstruction due to a postoperative band adhesion which was treated surgically. At the present time all are able to swallow without difficulty and are much improved.

The two patients with peptic esophagitis and stricture formation can both swallow without difficulty. The three patients with esophageal varices have had no further bleeding episodes, nor is there any evidence of varices in the interposed colonic segment.

Summary

Utilization of a segment of the colon has been carried out in 18 patients requiring substitution for either a diseased or congenitally atretic esophagus. The definitive procedure for the patients with esophageal atresia should be performed when the patient is either 1½ years of age or at least 20 lb. (9.1 kg.) in weight. The patient with irreversible stricture caused by lye should have substitutional therapy when it becomes apparent that dilation therapy is of only temporizing value. The patient with severe peptic esophagitis causing chronic blood loss as well as nutritional crippling should have formation of an adequate conduit as well as resection of the bleeding source. The patient who has bleeding esophageal varices is ideally treated by a portal-systemic type shunt. If this is impossible, then a direct attack on the esophageal varices is the remaining alternative. In our experience, suture ligation of varices has been of only temporary benefit. Resectional and substitutional therapy seems to be a more rational approach. At the present time we feel that the colon is the best structure for esophageal substitution.

300 Longwood Ave. (15) (Dr. Longino).

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EMOTION AND GASTRIC ACTIVITY

Charlyne T. Seymour, Ph.D.
and
Joseph A. Weinberg, M.D., Long Beach, Calif.

The emotional responses of 24 men were observed before and after vagotomy for duodenal ulcers. The surgical treatment was necessitated by hemorrhage, intractable pain, obstruction, or combinations of these conditions. The observations included fluoroscopy, roentgenograms, and determinations of the acidity and volume of gastric juice. Emotions were aroused by stressful interviews which proceeded with minimum delay to the patient's personal problems. These interviews elicited the same overt signs of psychological distress after the operation as they had before, but they no longer caused the increases of gastric secretion and motility seen in subjects with intact vagi. Since vagotomy was followed by healing of the ulcer in every instance, these findings strengthen the conviction that emotional influences play a role in the causation of duodenal ulcer.

Emotional tension is frequently expressed in somatic dysfunction, particularly of the gastrointestinal tract.[1] Psychotherapy aimed toward reducing the incidence of emotional distress has been considered to be an important adjunct to medical and surgical therapeusis of duodenal ulcers. This is a study of the effect of emotional stress on gastric activities before and after surgical interruption of the parasympathetic innervation of the stomach by vagotomy. Psychotherapeutic procedures were not used in this study; the patients received only medical and surgical treatment for their ulcers, except for the psychological aspects of the experimental work involved.

It is well established [2] that acid gastric juice is a *sine qua non* for the development and maintenance of a peptic ulcer. A potent source of corrosive gastric acid is the vagally innervated fundus. A complete vagotomy appears to abolish the nervous phase of gastric function and to reduce the humoral phase of gastric secretion.[3] Many investigators have observed that the average patient with duodenal ulcer secretes more gastric acid than the normal person, and, what is more important, he secretes more when no obvious stimulant is present. For example, there is continuous secretion throughout the night, which appears to account for the night pain so frequent in such patients.[4]

It has been suggested by many authors [5] that emotional tensions operating on either an unconscious or a subconscious level play an important part in the etiology and chronicity of duodenal ulcers. It may be that much of the material which is successfully repressed during waking hours is psychologically freed in sleep to stir the emotions and acts as an additional stimulant to the autonomic nervous system. Overactivity of this system has many effects on the gastrointestinal tract, among which are hypersecretion, hypertonicity, and hyperperistalsis.

Method of Study

Experimental procedures were designed to study the immediate effect of stressful psychological interviews before and after vagotomy. Previous work in this connection by Wolf [11] and Wolff and Levine [4] involved actual visualization of the human gastric mucosa during stressful interviews. Their patients did not undergo vagotomy, however.

The subjects were 24 men with duodenal ulcers selected at random from 150 persons referred for surgery after careful study by the medical and surgical gastroenterology services.

The criteria for such surgical referrals were hemorrhage, intractable pain, obstruction, or a combination of these conditions. The age range of the subjects was from 27 to 69 years. Duration of symptoms ranged from 1 to 30 years. The average period of hospitalization prior to surgical therapy was 2.8 months.

The patients were contacted individually previous to the experiment, and the general nature of the proposed procedures was described to them. Some ideas concerning the general problem areas of each patient were noted at that time, in order that the interviewer could proceed with minimal delay to the crux of the patients' difficulties during the period allotted for this phase of the study.

One day previous to operation a Levin tube was inserted nasally, under fluoroscopic observation, to be certain that the tube did not enter the duodenum. The hypersecretory tendency of patients with duodenal ulcer in the interdigestive periods (between meals and during the night) has been mentioned. This appearance of hydrochloric acid in the gastric juice is intermittent; in recognition of this periodic secretion it was realized that there might

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Staff Psychologist, Veterans Administration Hospital, and Associate Clinical Professor of Psychology, University of California at Los Angeles (Dr. Seymour); Chief, Surgical Service, Veterans Administration Hospital, and Clinical Professor of Surgery, University of California at Los Angeles Medical School (Dr. Weinberg).

be a fortuitous occurrence of "spontaneous" secretion after the introduction of an experimental procedure and that this might be interpreted erroneously as evidence of stimulation. Therefore, the interdigestive secretion was collected twice during the half-hour period just prior to the experiment and x-rays were taken. After this, two fasting gastric samples were obtained at half-hour intervals. The patient was then interviewed regarding emotionally charged personal problems. Each interview was geared individually in accordance with previous notes giving clues to problem areas. The third experimental gastric sample was withdrawn when overt evidence of psychological stress appeared to be optimal; e. g., pupillary dilatation, flushing or blanching, perspiration, tremors of lips or hands, restlessness, and other signs of tension. The patients invariably reported the presence of localized epigastric pain during most of this period, which occupied an average of 40 minutes. After 15 minutes of rest, a fourth sample was taken, fluoroscopy was done, and x-rays were taken. These procedures were repeated at two to three months and at one and one-half to two years after vagotomy. The gastric samples were checked for units of free acid and for volume. The statistical significances of preoperative and postoperative differences were estimated with use of a sign test.[6]

Results

Prior to vagotomy there was a reliable increase in gastric activity with emotional distress. Levels of significance obtained were free acid units $p=0.0001$ and volume $p=0.01$, indicating that the differences obtained were valid and were not chance occurrences. Motility and tonicity of the stomach increased noticeably, as evidenced by fluoroscopy and x-rays.

After vagotomy overt signs of emotional distress judged to be equivalent to that seen before surgery were easily aroused. There did not appear to be evidence of adaptation to problems; signs of physiological disturbance appeared at close to the same average time as previously. However, on questioning, there were no reports of epigastric pain. Neither free acid nor volume increased significantly at any of the trials. Radiologic evidence of decreased tonicity and motility of the upper region of the gastrointestinal tract was present.

The interview method of exciting emotional response appears to be a useful one in laboratory experiments of this type. It has the drawback of lack of standardization, but it has been found in this study and previously by Wolf[11] and his coworkers to have compensatory advantages.

Although patients, after vagotomy, reacted in a manner that was judged to be equivalent to their preoperative behavior as regards overt signs of psychological distress, the upper region of the gastrointestinal tract was not responsive and healing of the ulcer occurred in each instance.

Summary

The role of emotional tension in the etiology of gastrointestinal disorders is well established. A study was made of the role of such tension on gastric activities before and after surgical interruption of the parasympathetic innervation of the stomach by vagotomy.

Twenty-four men with duodenal ulcers were selected at random from 150 patients referred for surgical treatment. Ages ranged between 27 and 69 years and duration of symptoms from 1 to 30 years. A Levin tube was inserted nasally and x-rays were taken. Procedures were repeated at two to three months and at one and one-half to two years after vagotomy.

Samples were checked for free acid units and volume. The significance of preoperative and postoperative differences was estimated with use of a sign test. Prior to vagotomy there was a reliable increase in gastric activity with emotional distress. The motility and tonicity of the stomach increased noticeably as evidenced by fluoroscopy and x-rays. After vagotomy, overt signs of emotional distress judged to be equivalent to preoperative response were easily aroused. Neither the acid nor the volume increased significantly. Radiologic evidence of decreased tonicity and motility was present.

Although the patients reacted strongly to psychological stress in depth interviews after vagotomy, the upper region of the gastrointestinal tract was not responsive and healing of the ulcer occurred in each instance.

Veterans Administration Hospital (4) (Dr. Seymour).

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MASTER TWO-STEP EXERCISE TEST IN CLINICALLY UNSELECTED PATIENTS

Arnold J. Brody, M.D., White Sulphur Springs, W. Va.

There have been many publications on the Master two-step exercise test in clinically selected patients. Most are selected because of various types of chest pain or other symptoms that suggest coronary artery disease. Others are selected because of known coronary disease, and the exercise test is done and then compared with results in known healthy persons to prove or disprove its accuracy. If a large group of clinically unselected patients can be accumulated and followed for an adequate period of time, the material resulting should aid significantly in determining the reliability of the various electrocardiographic changes and the prognostic value of the Master exercise test.

The majority of patients seen at the Greenbrier Clinic are there for a periodic health examination and not because of specific symptoms, so this clinic is in a particularly good position to accumulate a group of clinically unselected patients. However, it is only fair to say that there is considerable sociological selection, in that the majority of the patients seen are middle-aged male business executives. Only patients who were followed for at least three years from the time of the original Master two-step exercise test were used in this analysis, which in itself involves some selection, but not clinical selection. Some of the patients had had follow-up examinations for as long as 10 years, but the average period of follow-up was slightly over 4 years.

The prognostic value of electrocardiographic tracings was investigated in the course of annual physical examinations of 756 business executives who had no history or symptoms suggestive of coronary heart disease. The age range was from 23 to 74 years. Electrocardiograms were obtained in each patient after the double Master two-step exercise test. The number of patients having abnormal electrocardiographic patterns when first examined was 280, and, of these, 32 later developed coronary artery disease. The remaining 476 had normal tracings, and only 20 developed coronary disease. The significant findings concerned the ischemic type of response pattern, which was found on 23 of the initial tracings. Sixteen (70%) of these patients later developed coronary artery disease. This finding is significant in view of published data on patients with known coronary disease, which show that 61.3% develop the ischemic pattern after the Master two-step test.

The Greenbrier Clinic does routine double Master two-step tests on all male patients. The method used is the standard 9-in. step as described by

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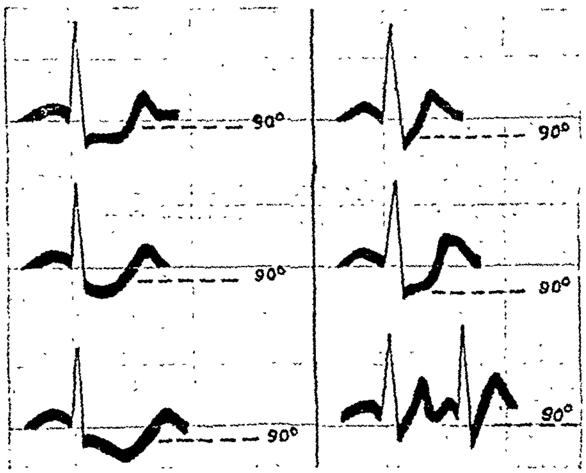
From the Greenbrier Clinic.

Master,[1] and the number of trips is timed and gauged according to his charts for age, weight, and sex. The only difference from Master's technique is that an electrocardiogram with standard leads 1 and 2 and unipolar chest leads V_2, V_4, and V_5 is taken immediately after exercise. There are no repeat electrocardiograms after time intervals. The results of the exercise tests have been divided and analyzed according to the following responses:

1. In the ischemic type of response, the S-T segment is depressed 0.5 mm. or more below the P-R or P-Q junction in such a fashion that it subtends an angle of 90 degrees or more with the vertical (see figure, *left*). Therefore, the S-T segment is depressed in a horizontal or sagging course as described by Myers and Talmers.[2] This differs from the progressive concave ascent of the S-T segment in junctional depression (see figure, *right*).

2. In junctional changes the S-T segment ascends progressively in a concave fashion. An attempt was made to separate the true junctional changes from the false depression of tachycardia where the auricular T wave is exaggerated and continues after termination of the QRS interval (see figure, *right*). In the first group of junctional changes the S-T segment was depressed at least 1.5 mm. below the P-R junction.



Left, types of ischemic depression. All are at least 90 degrees from vertical and 0.5 mm. below P-R junction. *Right*, types of junctional depression. All are less than 90 degrees from vertical. First two are true junctional depressions. Last is false depression due to tachycardia.

3. In the second group of junctional changes, the S-T segment depression was at least 0.5 mm. but under 1.5 mm.

4. T-wave changes included flat, diphasic, inverted T waves, or upright T waves in one or more leads, after exercise, that were previously flat.

5. The arrhythmias included frequent premature auricular and premature ventricular contractions, bundle-branch block, and one case of paroxysmal tachycardia after exercise.

6. In the patients with abnormal resting electrocardiograms that showed changes after exercise, most of the resting electrocardiograms showed flat, diphasic, or shallow inversion of T waves in several leads. Some showed bundle-branch blocks. The changes after exercise included the five changes mentioned above. Many of these showed T waves that became upright after exercise but which were isoelectric in the resting electrocardiogram.

Analysis of Results

The total number of patients who were given double Master exercise tests from July, 1948, to March, 1955, and were followed three years or more after the first examination was 756. Of this number, a total of 280 had positive responses, using Master's original criteria [3] of any S-T depression of 0.5 mm. or over, upright, flat, or inverted T-wave changes, arrhythmias, and conduction defects or heart block after exercise. Although this is a high number, it will be seen in the subsequent analyses that this total number means very little. For the total 280 patients with positive test results, the age range was from 32 to 69 years, with a mean age of 53. Of these, 32, or 11.4%, developed classic angina pectoris, coronary insufficiency, or definite myocardial infarction within the 3-to-10-year follow-up. Again, in view of the subsequent analyses, this percentage has little meaning in itself.

There were a total of 476 patients who had negative exercise test results and were followed for the 3-to-10-year period. They had an age range of 23 to 74 years, with a mean age of 49. Of this group, 20, or 4.2%, developed classic angina pectoris, coronary insufficiency, or definite myocardial infarction.

Ischemic Responses.—In a total of 23 of the 280 positive Master tests the patients had typical ischemic responses. The age range of these patients was 36 to 63 years, with a mean age of 54. Six patients subsequently developed myocardial infarction, and 10 developed classic angina pectoris, so a total of 69.5% developed definite coronary disease.

Seven patients remained asymptomatic, and of this group five subsequently developed abnormal resting electrocardiograms, four of which showed abnormal nonspecific T-wave changes and one change compatible with left ventricular hypertrophy. Two of these seven patients continued to have normal resting electrocardiograms; one continued to show ischemic depression on the double Master exercise test but showed normal results after a single test, and the other showed a change from ischemic depression after exercise to a 1.5-mm. junctional depression after exercise. The latter patient was obese and in the interim lost approximately 30 lb. (13.6 kg.).

Junctional S-T Segment Depression of 1.5 Mm. or Over.—A total of 23 patients in the group showed junctional S-T segment depression of 1.5 mm. or over; their ages ranged from 35 to 52 years, with a mean age of 50. Three patients subsequently developed myocardial infarctions; one died. Two patients subsequently developed classic angina pectoris. Therefore, a total of 21.7% developed definite coronary disease in this group.

Of the other 18 patients, 7 showed no change with a continuing junctional S-T segment depression of 1.5 mm. or over after exercise. Five subsequently had a negative Master exercise test result. Three subsequently had abnormal resting electrocardiograms, consisting of abnormal T waves of nonspecific patterns. For two patients the exercise test results changed to show lesser degrees of junctional depression (under 1.5 mm.), and in one the results remained unchanged after a double Master exercise test, but a single test showed negative results.

Junctional S-T Depression Between 0.5 and 1.5 Mm.—A total of 161 patients, with an age range of 30 to 67 years and a mean age of 50, showed junctional S-T depression between 0.5 and 1.5 mm. Of this group, four subsequently developed classic angina pectoris and there were no subsequent infarctions in the follow-up period, giving a total of 2.5% who developed coronary disease.

Of the remaining patients, 79 had negative Master exercise test results subsequently, 62 remained unchanged, 7 developed abnormal resting electrocardiograms (nonspecific abnormal T-waves changes), 5 developed junctional depression over 1.5 mm. in depth, and 4 subsequently developed ischemic depression after exercise.

Arrhythmias.—A total of 24 patients, with an age range of 32 to 66 years and a mean age of 51, developed arrhythmias. Three patients subsequently developed classic angina pectoris, of these, one had bigeminal premature ventricular contractions, one had transient right bundle-branch block, and one had transient left bundle-branch block after exercise; none developed subsequent myocardial infarctions, giving a total of 12.5% who developed coronary disease.

Among the other patients, there were 11 who developed premature ventricular contractions after exercise; for 7 of these the results subsequently became negative and in 4 remained unchanged. Nine patients developed premature auricular contractions after exercise; six of these subsequently showed negative results of exercise tests. In two patients, the results of the test remained unchanged, and one developed junctional depression of less than 1.5 mm. One patient developed transient auricular paroxysmal tachycardia in one lead after exercise, and in the following years the results of the tests became negative.

T-Wave Changes Only.—There were a total of 27 patients who showed T-wave changes only; their age range was 38 to 67 years, with a mean age of 54. Most of the T-wave changes included significant reduction of amplitude in one or more leads after exercise. Generally, the T waves became flat-diphasic or flat or developed shallow inversion in two or more leads. In only one case was there inversion of over 4 mm. in leads V_4 to V_6; this was in the only patient who developed classic angina pectoris, so only 3.6% of this group developed definite coronary disease.

Of the other patients, 12 subsequently showed negative exercise test results; 6 showed permanent abnormal resting electrocardiograms, five of which showed nonspecific T-wave changes and one a left bundle-branch block. In five patients, the exercise test result remained unchanged in the follow-up period. Two patients subsequently developed junctional depression under 1.5 mm., and one patient developed junctional depression of 1.5 mm. or more.

Abnormal Resting Electrocardiograms for Patients Showing Positive Responses After Exercise.—A total of 22 patients had abnormal resting electrocardiograms and positive results after exercise. Their ages ranged from 41 to 66 years, with a mean age of 55. Two patients subsequently developed myocardial infarction; both died. In both of these, the resting tracing showed nonspecific abnormal T-wave changes. After exercise one showed ischemic depression; the other showed upright T waves after exercise when they had been previously flat. Another patient subsequently developed angina pectoris. In this patient the resting tracing showed shallow inversion of T waves that became more inverted after exercise. This makes a total of 13.6% who developed coronary disease.

Of the other patients, 12 had abnormally flat T waves and developed upright T waves in one or more leads after exercise. Nine remained unchanged in the follow-up period of three or more years, and in three cases the results of exercise tests subsequently returned to normal. Three patients with nonspecific T-wave changes developed junctional depression of at least 1.5 mm. after exercise, and this remained unchanged in the follow-up period. Two patients had resting electrocardiograms compatible with left ventricular hypertrophy and strain and ischemic changes developed after exercise; these remained unchanged in the follow-up period. Two patients had right bundle-branch block. One of these developed ischemic changes after exercise, and one developed inverted T waves in the left chest lead after exercise. Both of these remained unchanged in the follow-up period.

Comment

It is evident from this analysis that the ischemic type of response had definite significance. In this group, 69.5% of the patients subsequently developed definite coronary disease in the 3-to-10-year follow-up period. It is worthwhile to compare this figure with that of clinically selected patients with known coronary disease. One of the largest groups is that of Russek,[4] who analyzed 186 patients with known coronary disease; 61.3% developed an ischemic type of response after a double Master exercise test. On the other hand, when Russek exercised 108 known healthy patients, 19.4% had positive Master test results according to Master's total criteria, but none of these had ischemic S-T segment depression. Robb and associates[5] gave double Master exercise tests to 69 patients with known coronary disease; 50.7% had ischemic changes. Although these figures are on clinically selected patients with known coronary disease, they are similar to those for the clinically unselected patients who were followed for 3 to 10 years for this report.

In analyzing the junctional changes over 1.5 mm., it cannot be dogmatically stated that these changes are significant, but it is probably more than chance that 21.7% did develop coronary disease. This is not in disagreement with Myers and Talmers,[2] who stated that if junctional depression is deep enough and not due to tachycardia it can be due to subendocardial ischemia.

In this study, it is evident that junctional changes under 1.5 mm. had no significance. Only 2.5% of the patients subsequently developed coronary disease, as compared to the control group, who showed negative results of the tests and of whom 4.2% developed coronary disease. Obviously, this group had no more coronary disease than the group with negative exercise tests. Four of these patients did subsequently develop ischemic depression after exercise, which according to this study has a poor prognosis, but even if this group is added to the number who developed coronary disease, it makes a total of only 5%, which is still not significantly different from the control group. These results are very different from Master's statements that any depression 0.5 mm. or over has definite significance.[1] There is only partial agreement with the work of Robb and associates.[5] They showed that the patients with ischemic response had an incidence of coronary occlusion of 79 per 1,000, while those with junctional response had a considerably lower incidence (35 per 1,000) but yet a *significantly higher incidence than the* group of those with negative test responses, who had an incidence of coronary occlusion of 9 per 1,000. However, they did not separate the junctional responses by degree but tabulated all junctional depression of 0.5 mm. or over in one group.

In the group with arrhythmias, the patients who developed coronary disease had transient bundle-branch blocks or bigeminal premature ventricular contractions after exercise. Since there were only three such cases, little can be said from this. However, it is evident that premature ventricular contractions and premature auricular contractions of no definite pattern had no significance.

The only patient who developed coronary disease in the T-wave change group had T-wave inversion of 4 mm. in leads V_4 to V_6. There was no correlation between development of subsequent coronary disease and minor T-wave changes.

Since an abnormal resting electrocardiogram may affect the patient's prognosis, it is difficult to say how significant the changes were that occurred in this group. It is interesting to note that two patients who had ischemic changes after exercise and who *did not subsequently develop coronary disease* had patterns of left ventricular hypertrophy and strain, which classically show an ischemic type of depression in the resting electrocardiogram.

Summary and Conclusions

Double Master two-step exercise tests were given to a group of 756 clinically unselected male patients who were followed for periods of 3 to 10 years. Ischemic changes after exercise, wherein the S-T segment is depressed horizontally or downward at least 90 degrees from the vertical and 0.5 mm. or more below the P-R or P-Q junction, had definite significance in diagnosis of potential clinical coronary disease. True junctional S-T segment depression over 1.5 mm. in depth, not due to tachycardia, was suggestive of potential coronary disease. On the other hand, there was no correlation between development of coronary disease and junctional S-T segment depression under 1.5 mm. in depth, minor T-wave changes, or minor transient arrhythmias such as premature auricular or premature ventricular contractions without a definite pattern.

Miss Dreama Morgan assisted in gathering data for this report, and Mr. Howard Southern drew the electrocardiograms.

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PROPHYLACTIC ANTIBIOTIC THERAPY IN INFANTS BORN AFTER PREMATURE RUPTURE OF MEMBRANES

Sidney P. Kent, M.D.
and
Gilder L. Wideman, M.D., Birmingham, Ala.

The death rate among infants born after premature rupture of the fetal membranes in a hospital rose sharply from 29 per 1,000 in 1954 to 144 per 1,000 in 1958. Various factors known to affect neonatal mortality in other situations were eliminated by analysis of the data until it appeared that the rise in death rate had followed the institution of a program of prophylaxis with antibiotics. Among 160 newborn infants who received such prophylaxis from January to May, 1958, 7 deaths occurred among 97 who received chloramphenicol with erythromycin, 5 among 8 who received chloramphenicol, erythromycin, and penicillin, and 5 among 5 infants who received chloramphenicol, erythromycin, penicillin, and streptomycin. Among the infants who died the characteristic syndrome included anorexia, lethargy, respiratory distress, a shock-like state, and a dusky gray appearance. The data were not sufficient to identify a single antibiotic as the sole cause, but no further cases of "gray sickness" occurred after the use of chloramphenicol was discontinued.

The neonatal death rate is usually slightly higher at University Hospital than at other hospitals in Jefferson County, probably because of a higher percentage of indigent patients, but during the last six months of 1957 and the first six months of 1958 this death rate rose significantly (fig. 1). The neonatal death rate of all the other hospitals in Jefferson County was relatively constant during this period. As there was no obvious cause, such as a nursery epidemic, for this rise in neonatal mortality, it was decided to evaluate the effectiveness of prophylactic administration of antibiotics in newborn infants during the period. Prophylactic antibiotic therapy had been used in the University Hospital to a limited extent for several years. During the last half of 1957 and the first part of 1958 three categories of indigent patients received prophylactic therapy: certain premature infants, infants born after unsterile delivery, and infants born after premature rupture of the maternal membranes. The last-named two groups routinely received some type of prophylactic antibiotic therapy. The largest group consisted of those born after premature rupture of the membranes, and for this reason it was selected for study.

Materials and Method

The charts of all patients who delivered at the University Hospital during the first four months of 1954, a period when prophylactic antibiotic therapy in newborn infants was infrequently used, and for the first four months of 1958, a period when prophylactic antibiotic therapy was quite frequently used, were reviewed. The chart of each mother giving birth to a living child after premature rupture of the membranes was set aside and matched with her infant's chart. The following data were recorded from each mother's chart: age, race, diseases, obstetric complications, type of delivery, antibiotics received before delivery, length of rupture of the membranes, whether the membranes ruptured spontaneously or artificially, and number of prenatal clinic visits made. The birth weight, sex, race, type of prophylactic therapy, if any, symptoms, obstetric injuries, age at death, and autopsy findings, if available, were recorded for each infant. Antibiotic therapy was considered prophylactic if started within six hours after birth and before the onset of any clinical signs of infection. Six hours was the criterion used on the pediatric service during the period under study for ,premature rupture of the membranes, so the same criterion was used in this study.

The neonatal deaths in both groups of patients, those from 1954 and those from 1958, were further checked through the vital statistics bureau of the Jefferson County Public Health Department, because the infants' stay in the hospital varied considerably (1 to 30 days), particularly for 1954, and was usually only a fraction of the 28-day neonatal period. Several neonatal deaths in both 1954 and 1958 were found in this way.

Results

Data for both private and indigent patients were studied, but the results to be presented include only those from indigent patients (table 1). A comparison of indigent patients who did not receive prophylactic therapy with those who did is more valid than a similar comparison with private pa-

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From the departments of pathology and obstetrics and gynecology, University of Alabama Medical Center.

tients, because the private patients during 1958 did not routinely receive prophylactic therapy with antibiotics.

The death rate in the 148 infants born after premature rupture of the maternal membranes in 1954 who did not receive prophylactic therapy was 29 per 1,000 (table 2). When compared to the over-all neonatal death rate among indigent patients for the same period, 26 per 1,000, little difference is noted. This suggests that premature rupture of the membranes, at least in this group, did not appreciably affect mortality.

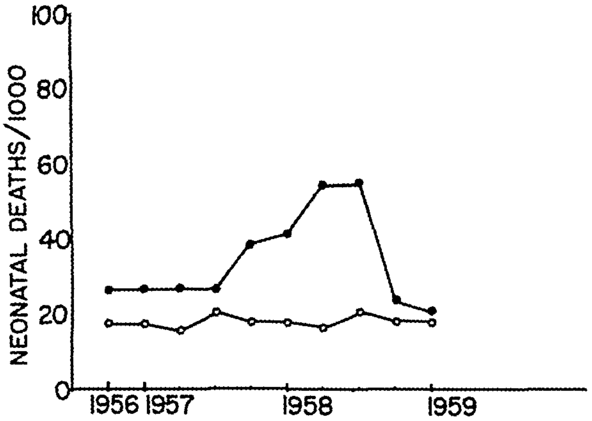

Fig. 1.—Neonatal death rates for University Hospital (*closed dots*) and all other hospitals in Jefferson County (*open dots*) for 1956, 1957, and 1958.

The neonatal death rate in the group receiving prophylactic therapy in 1958 was 144 per 1,000. This is almost five times the death rate of the group in 1954 that did not receive prophylactic therapy. The over-all neonatal death rate in indigent patients during the first four months of 1958 was 69 per 1,000 or slightly less than half the rate in the group receiving prophylactic therapy.

The difference in the death rates of the prophylactically treated and nontreated groups are statistically significant ($p<0.002$). The obvious difference in the two groups was the use of antibiotics. Other factors known to affect neonatal mortality have been studied (table 3). The incidence of prematurity in the two groups was the same. The fact that almost half of those who died after prophylactic therapy were full-term infants further indicates that prematurity does not explain the rise in neonatal mortality (table 4). The relative incidences of prolonged rupture of the membranes (24 hours or more) was not significantly different. The racial composition of the two groups was also similar (table 3). The latter is of importance, as neonatal mortality is higher among Negroes in this area. No other obvious difference between the prophylactically treated and the nontreated groups, such as age, parity, prenatal clinic visits, or maternal disease, was noted.

Table 1.—*Premature Rupture of Membranes in Indigent Patients*

	Jan.-May, 1954	Jan.-May, 1958
Total births	988	1,070
Births after premature rupture of the membranes	148	179
Patients receiving prophylactic antibiotic therapy	11	160
Patients with premature rupture but no prophylactic antibiotic therapy	137	19

Table 2.—*Neonatal Death on Indigent Service*

	Jan.-May, 1954		Jan.-May, 1958	
	No.	Per 1,000	No.	Per 1,000
Total live births	988		1,070	
Total deaths	24	26	74	69
Premature rupture with no prophylactic therapy	148	...	...	...
Premature rupture with prophylactic therapy	...	...	160	...
Deaths with no prophylactic therapy	4	29	...	...
Deaths with prophylactic therapy	...	...	23	144

In addition to the 23 patients in the group given prophylactic treatment with antibiotics who died were 8 other infants who showed a characteristic clinical syndrome but did not die. Of the 23 infants who died 14 showed a similar clinical picture. These infants appeared normal until the second to fifth day after birth (table 4). They then typically stopped eating and became hypoactive and lethargic. Respiratory distress with rapid, shallow, irregular respirations was quite common. The dusky gray appearance of these infants was so characteristic that the pediatric residents working in the nursery at the time referred to the syndrome as the "gray sickness." The appearance of these infants suggested to several observers that the infants were in shock. Most of them presented a clinical picture of gram-negative septicemia. Blood cultures during life and culture of the lungs in those who came to autopsy were done routinely but no positive cultures were found in the 14 infants with the above symptoms. Virus studies of blood and lungs obtained at autopsy also failed to reveal pathogens.

Table 3.—*Prophylactically Treated Group (1958) Versus Nontreated Group (1954)*

		No.	%
1954*	Negroes	103	77
1958†	Negroes	128	80
1954	Membranes ruptured for 24 hr. or more	53	39
1958	Membranes ruptured for 24 hr. or more	57	36
1954	Premature births	24	18
1958	Premature births	28	18

* Total patients=137.
† Total patients=160.

Comment

Prophylactic antibiotic therapy has been tried in a number of situations in medicine and has been proved valuable in very few. Prophylactic treatment with penicillin has been shown to decrease the rate of recurrence in patients who have had rheumatic fever.[1] The patients were being protected against a single organism whose sensitivity was known. The use of prophylactic antibiotics to protect surgical patients, children with measles or upper respiratory infections, and unconscious patients from secondary bacterial infection has not been successful.[2] In these situations the patients must be protected from a variety of organisms with unknown sensitivities. Prophylactic use of antibiotics after premature rupture of the membranes was more in common with the latter use, since the vaginal flora are quite varied.

TABLE 4.—*Analysis of Twenty-three Deaths in Prophylactically Treated Group*

Case	Race, Sex	Birth Weight, Gm.	Length of Rupture of Membranes, Hr.	Age at Onset of Symptoms, Days	Antibiotics Administered*	Age at Death, Days	Findings at Autopsy
1	N, M	2,500	24	2	Chloramphenicol, erythromycin	2	Lobular pneumonia, slight†
2	N, M	2,020	56	0	Chloramphenicol	2	None
3	N, M	2,460	8	5	Chloramphenicol, *erythromycin*	5	None
4	N, M	3,912	26	4	Chloramphenicol, penicillin	4	None
5	N, M	2,722	8	5	Chloramphenicol	5	None
6	N, M	1,417	7 days	4	Chloramphenicol, erythromycin	4	None
7	N, M	3,033	6	5	Chloramphenicol, erythromycin	5	Atelectasis, minimal†; fatty change in liver
8	N, M	2,728	48	3	Chloramphenicol, erythromycin, penicillin	4	None
9	N, M	2,892	12	5	Chloramphenicol, erythromycin-neomycin, penicillin	5	Yes†
10	N, M	2,420	12	5	Chloramphenicol	8	Bronchial pneumonia, bilateral
11	N, M	3,065	6½	3	Chloramphenicol penicillin, neomycin, streptomycin	20	None
12	N, F	2,750	22	6	Chloramphenicol, penicillin, streptomycin, novobiocin, neomycin	16	Yes†
13	C, M	1,817	6	5	Chloramphenicol, erythromycin, penicillin	6	Yes†
14	C, M	2,098	60	4	Chloramphenicol, erythromycin, penicillin	6	Yes†
15	C, F	1,440	7 days	0	Chloramphenicol, *penicillin, streptomycin*	6½ hr.	None
16	C, F	1,966	7 days	3	Chloramphenicol, erythromycin, penicillin	6	None
17	C, M	1,899	19	2	Chloramphenicol, penicillin	2	Atelectasis, slight,† petechial hemorrhages in lungs
18	N, M	1,916	43	5	Chloramphenicol, erythromycin, penicillin	6	None
19	C, F	3,062	17	2	Chloramphenicol, erythromycin, penicillin	2	None
20	N, M	2,540	17	3	Chloramphenicol, erythromycin	4	Truncus arteriosus
21	N, F	2,260	4½ days	3	Chloramphenicol, penicillin, streptomycin, neomycin, novobiocin	4	None
22	N, F	1,871	39	4	Chloramphenicol, penicillin, streptomycin	5	None
23	N, F	2,700	6	5	Chloramphenicol	5	Petechial hemorrhages in lungs and stomach†

* Prophylactic antibiotics were administered within six hours of birth and were continued for five to seven days. The dosages used varied: chloramphenicol (Chloromycetin), 50 to 100 mg. every 8 or 12 hr.; erythromycin (Ilotycin), 50 mg. every 8 hr.; penicillin, 50,000 to 150,000 units every 12 hr.; streptomycin, 30 to 125 mg. every 12 hr.; neomycin, 10 to 15 mg. every 8 or 12 hr.; and novobiocin, 50 mg. every 8 to 12 hr.

† No anatomic lesion noted or no adequate explanation for symptoms and death.

In considering ways that prophylactic antibiotic therapy in the newborn infant may contribute to an increase in mortality, three possibilities come to mind. First, some of the antibiotics were given by injection, which provides an additional portal of entry for bacteria. Second, extensive use of antibiotics may result in the development of resistant strains of bacteria in the nursery. Finally, one or more of the antibiotics used may be toxic to the newborn infant. Newborn infants may not be prepared as well metabolically as are adults to tolerate one or more of the antibiotics used. If either of the first two factors were operating one would have expected to see evidence of infection in infants coming to autopsy. The demonstration of infection in the infant autopsies during this period was infrequent. Evaluation of toxicity of the antibiotics used is complicated because combinations of antibiotics were usually employed (table 5). Four antibiotics in eight different combinations were used in the prophylactic program. Also, additional antibiotics were added to the treatment schedules of some infants during the course of their illness. However, chloramphenicol was the drug most extensively used; 145 of the 160 infants who had prophylactic therapy received chloramphenicol. Furthermore, all of the infants who died, as well as the eight with the "gray sickness" who lived, received chloramphenicol in doses ranging from 100 to 300 mg. every 24 hours. Erythromycin was the next most commonly used drug. It was given only with chloramphenicol. There were several infants who died and others who had the "gray sickness" who did not receive *erythromycin.* Further correlation between the increase in the use of chloramphenicol in the nursery and the neonatal death rate is striking (fig. 2). The relative frequency of the use of chloramphenicol in the program of prophylactic therapy was determined by reviewing 20 or 25 charts, selected at random by the record room, of infants receiving prophylactic therapy for each month during 1957 and 1958.

TABLE 5.—*Antibiotic Combinations Administered in 160 Newborn Infants January-May, 1958*

Antibiotics Received	No. of Patients	Deaths
Chloramphenicol	5	1
Chloramphenicol and erythromycin	97	7
Chloramphenicol, erythromycin, and penicillin	8	5
Chloramphenicol, erythromycin, penicillin, and neomycin*	1	1
Chloramphenicol, erythromycin, and neomycin*	2	1
Chloramphenicol, erythromycin, neomycin, and novobiocin*	2	1
Chloramphenicol and penicillin	4	2
Chloramphenicol, penicillin, and streptomycin	11	2
Chloramphenicol, penicillin, streptomycin and neomycin*	1	1
Chloramphenicol, penicillin, streptomycin, *neomycin, and novobiocin**	1	1
Chloramphenicol, penicillin, streptomycin, neomycin and novobiocin	3	1
Chloramphenicol, erythromycin, penicillin, and streptomycin	5	5
Penicillin and streptomycin	12	...
Penicillin	1	...
Penicillin, streptomycin, and novobiocin*	1	...
Neomycin	1	...

* Except in one case neomycin and novobiocin were added late in the course of illness; that is, they were not used prophylactically.

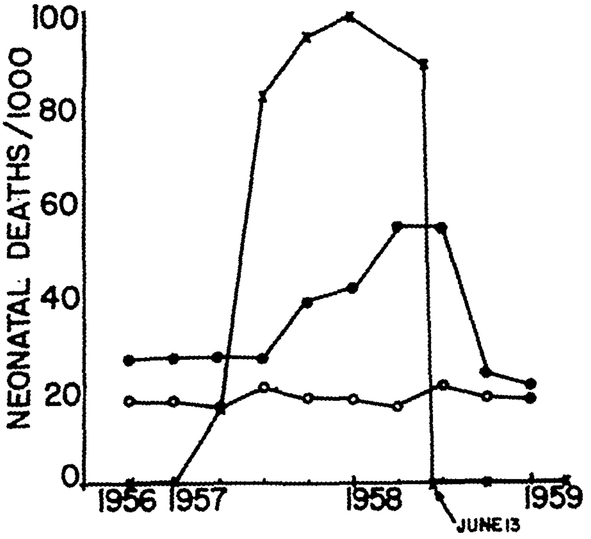

Fig. 2.—Neonatal death rates for University Hospital and all other hospitals in Jefferson County for 1956, 1957, and 1958, with percentage of group in University Hospital nursery receiving prophylactic therapy with chloramphenicol (*crosses*) added.

The rise in the neonatal death rate followed the increase in the use of chloramphenicol in the prophylactic program. When the use of chloramphenicol in the nursery was discontinued on June 13, 1958, the neonatal death rate dropped back to and remained at about the level present before the use of chloramphenicol. Several changes were made in the operation of the nursery during the spring of 1958, in an attempt to lower the neonatal death rate, which makes this portion of the two curves shown in figure 2 more difficult to evaluate. However, there was no notable change in the operation of the nursery in July, 1957, when the rate began to rise, other than the increased use of prophylactic therapy with antibiotics and the change from penicillin and streptomycin to chloramphenicol and erythromycin as the recommended drugs. Furthermore, the "gray sickness" has disappeared from the nursery since use of chloramphenicol was discontinued on June 13, 1958.

TABLE 6.—*Antibiotic Therapy in Infants Born to Indigent Patients in March, 1958*

	Patients, No.	Deaths	
		No.	per 1,000
Total deliveries	297	25	84
No antibiotic therapy	205	4	20
Total receiving antibiotic therapy	92	21	226
Chloramphenicol therapy	84	19	226
Prophylactic antibiotic therapy	79	16	202

The role that prophylactic antibiotic therapy may have played in the over-all increase in neonatal mortality is of interest. When the over-all neonatal death rate of the first four months of 1954, 26 per 1,000, and 1958, 69 per 1,000, are compared, it should be kept in mind that the latter includes the group of those born after premature rupture of the maternal membranes and given prophylactic therapy, with its high mortality. If this group is simply removed from the total, the over-all rate drops to 56 per 1,000. It also includes two other groups of infants given prophylactic therapy; infants having nonsterile deliveries and certain premature infants. To gain some insight into the over-all frequency of prophylactic therapy during the first four months of 1958, the charts of all the infants born in March, 1958, were reviewed (table 6). It is evident that almost one-third of the infants born in this period received antibiotic therapy. In most instances this was prophylactic therapy which usually included chloramphenicol. Furthermore, 19 of the 25 infants dying during this month received chloramphenicol. These data suggest that if chloramphenicol therapy is not well tolerated by newborn infants, its use was extensive enough during this period for it to have been a major factor in the over-all rise in neonatal death rate at the University Hospital.

Summary

The neonatal death rate in a group of 148 infants born after premature rupture of the maternal membranes who received no prophylactic antibiotic therapy was determined and compared to that of a similar group of 160 infants who did receive such therapy. The death rate in the latter group was 144 per 1,000, as compared to 29 per 1,000 in the former. There is a possibility that the increase in neonatal mortality was due to chloramphenicol toxicity, but the evidence presented does not prove a relationship between the increased death rate in the infants receiving prophylactic therapy and chloramphenicol therapy; however, it is sufficient to suggest the need for some evaluation of the toxicity of chloramphenicol in the newborn infant.

1919 Seventh Ave. South (3) (Dr. Kent).

The bacterial culture and virus studies were performed by Drs. Charles Winkler and Robert Francis, Department of Microbiology, respectively. Dr. Sara Finley, Department of Pediatrics, supplied important data.

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CLINICAL NOTES

ISOSENSITIZATION TO THE U FACTOR

Calvin C. Sampson, M.D., Constance Thomas, B.S., M.T.
and
Seabron Griffin, B.S., Washington, D. C.

Reported instances of sensitization to the U factor are extremely rare; in fact, we could find only three cases reported in the literature. In 1953 Wiener and co-workers [1] reported a fatal hemolytic transfusion reaction caused by sensitization to a previously unreported blood factor which they designated as U. Greenwalt and co-workers,[2] in 1954, and Wiener and Unger,[3] in 1958, reported the second and third cases respectively. All of these cases occurred in Negroes. We believe that the case presented here represents the fourth reported instance of isosensitization to the U factor.

Report of a Case

A 58-year-old Negro man was admitted to Freedmen's Hospital on March 19, 1959, for treatment of a malignancy of the prostate gland. On admission, a blood count showed 8.3 Gm. of hemoglobin per 100 cc., 27% hematocrit, and 11,000 white blood cells per cubic millimeter, with 66% neutrophils, 27% lymphocytes, and 5% eosinophils. The patient denied having received previous blood transfusions. Two pints of blood was requested to help correct the anemia. Initial blood bank studies showed that the patient's blood was group O, type Rh_0 (cDe). Both donors were of similar type. Routine crossmatches, performed in saline solution, albumin, and antihuman globulin, were compatible and on March 20, 1959, 1,000 cc. of blood was given, with no noticeable reaction. Nine days after the transfusions more blood was requested. At this time, however, there was agglutination on the major side of the albumin crossmatch with numerous specimens of blood belonging to the patient's blood group. The saline and antihuman globulin determinations were compatible. Results of the indirect Coombs test and tests for cold and warm agglutinins were negative. Several attempts to secure compatible blood during the next few weeks failed. Four weeks after transfusion the result of the indirect Coombs test became positive with a titer of 1:128, and the albumin titer was 1:16. Agglutination was still negative in saline solution. Since these determinations showed presence of a blocking antibody, tests for the M, N, P, Duffy, Cellano, and Kell factors were performed. Since results of these, all being positive, were not revealing, a specimen of the patient's blood was sent to the National Institutes of Health, Bethesda, Md., for further testing. Here it was shown that the patient was U-negative and had antibodies to this factor. Subsequent testing showed that the donors were U-positive. Attempts were then made to secure U-nega-

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From the blood bank of Freedmen's Hospital and Department of Pathology, Howard University, College of Medicine.

tive blood but all were unsuccessful. Two months after hospitalization and surgery the patient showed improvement, and plans were made for his discharge.

Comment

The U factor is almost universally present in human erythrocytes. Studies by Wiener and co-workers [4] showed that every blood specimen from a series of 1,100 Caucasians contained the U factor, whereas among those from 989 Negroes 12 did not have the U factor. Further studies showed that this factor is not related to the A-B-O, Rh-Hr, Duffy, Kidd, Lutheran, Lewis, or P blood-group systems. It was noted, however, that all 12 U-negative persons had blood of type N or MN, which suggested a possible relationship to this system. Sanger and co-workers [5] noted that all U-negative persons lacked the S and s factors which belong to the MNS system. This finding proved that the U factor is a part of the MNS system. Wiener and co-workers [1] reported that the U factor is inherited as a simple mendelian dominant.

This case is similar to those previously reported in that the patient was Negro and had type MN blood. There was no apparent relationship to other blood-group systems. The antibody found was of the univalent or blocking type, as was noted in the case of Greenwalt and co-workers [2] and in the second case of Wiener and Unger.[3]

It is of interest to note that 1.2% of Negroes tested are U-negative. Because of this fact, many problems are readily apparent. Hospitals treating Negro patients should be charged with the responsibility for proper selection of blood donors to prevent immunization to the U factor. Sensitization to this factor in U-negative Negro women with U-positive husbands may be a cause of erythroblastosis fetalis in their babies. Fatal hemolytic transfusion reactions may occur, as noted in the case reported by Wiener and co-workers.[1] Since agglutination was observed in our case on a routine albumin crossmatch, the possibility of a fatal hemolytic reaction was averted. Once these persons are sensitized, they must receive U-negative blood only, and this presents a problem, due to the scarcity of U-negative donors. Since blood banks do not routinely test for this factor, it behooves every clinician treating Negro patients to be discerning and judicious in ordering blood transfusions.

Help in identifying the antibody and confirmation of earlier findings were given by Dr. John S. Fordtran of the National Institutes of Health.

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CONTINENTAL BREAKFASTS FOR HOSPITAL PATIENTS.—Like most hospitals, St. Luke's [in Jacksonville, Fla.] was faced with the problem of awakening the patient early for baths and medications, and then keeping him happy until the breakfast service started at 8 a.m. W. E. Arnold, executive director of the 210-bed hospital, worried about the problem until a chance business meeting in New York gave him the solution. An early riser, Mr. Arnold was delighted to find an insulated container of hot coffee and a hard roll with butter and jelly deposited at daybreak in the service slot of his hotel room. A comparable solution could be effected, he felt, in the hospital by young girls serving pots of hot coffee and buns to all patients who wanted an early snack. In the spring of 1954 final plans for a "continental breakfast cart" were put into operation. Two high school girls were employed . . . to come in at 5:30 in the morning to prepare the carts, one for each of the two floors. By 6 o'clock the girls were dressed in white pinafores over blue dresses and had the carts ready for service on the floors. Each cart is equipped with an insulated container of hot coffee, one of hot water for tea, a warmer filled with hard rolls and sweet rolls, butter and jelly. . . . A cup of steaming hot coffee and a roll are served to each patient who asks the night before to be put on the pre-breakfast list. Service is not made, of course, if chart orders conflict. . . . The average daily cost of this service is approximately 12 cents per person. "We feel that this is a small price to pay for a contented patient," Executive Director Arnold said. "The nurses and doctors find the patient more cooperative; the dietary department is well repaid for the extra effort by the enthusiastic reception the service receives."—Continental Breakfast Builds Good Will at Low Cost, *Hospitals,* May 16, 1959.

SPECIAL ARTICLE

PRIMER ON THE RHEUMATIC DISEASES

PART I

Prepared by a Committee of the American Rheumatism Association

This is the fifth edition of the Primer on the Rheumatic Diseases, previous editions having been published in 1934, 1942, 1949, and 1953. This publication presents basic material concerning rheumatic diseases in as simple and concise a form as is consistent with adequate coverage, bearing in mind the particular needs of the general physician and the student. The voluminous and rapidly expanding literature is not cited because of the condensed nature of the primer. The 12th "Review of American and English Literature," the previous "Reviews," and textbooks by outstanding authorities in the field are available in medical libraries for more extensive reading and background. The new journal *Arthritis and Rheumatism*, now the official organ of the American Rheumatism Association, and the *Annals of the Rheumatic Diseases*, published in London, provide the clinician with an abundant source of current articles on these subjects.

The terms "rheumatism" and "rheumatic diseases" are now accepted as synonymous and are used to indicate any painful disorder in which the principal symptoms are related to the joints or their anatomic supporting structures. Rheumatic fever; various types of degenerative, inflammatory, and metabolic arthritis; a large group of ill-defined conditions such as fibrositis, tendinitis, myositis, and neuritis; and the so-called collagen or connective tissue disorders are included in this category and are the chief concern of this primer. Certain other diseases which present secondary manifestations referred to articular structures are included more briefly for differential diagnostic purposes.

Incidence of Rheumatic Disease

A full-scale population sampling to discover the prevalence of various diseases and the influences of environmental factors has not been accomplished in the United States since 1937. This sorely needed study is contemplated for 1959.

Previous studies have revealed that articular and nonarticular rheumatic diseases, exclusive of rheumatic heart disease, disable almost 10% of the population, 10 times as many as diabetes, 7 times as many as cancer, and twice as many as heart disease. The results of all such surveys are, of course, open to criticism. Large population surveys, however well planned from the statistical and representative standpoints, lack diagnostic accuracy. Clinic, hospital, and private office surveys, on the other hand, provide more accurate diagnoses but may lack representative sampling. Despite this, any investigation indicates that the rheumatic diseases are a formidable group of illnesses, from the standpoint of the number of persons affected and the total disability engendered.

The Canadian sickness survey of 1950-1951 revealed that 225,000 persons, of the total population of 15 million, had arthritis or rheumatism. Of these 50,000 were severely or totally disabled solely or primarily because of rheumatic diseases. This incidence is considerably lower than estimates in this country, apparently because a large number of mild or nondisabling rheumatic disorders and rheumatic fever were not included.

Information gathered by lay interviewers in five U. S. Public Health Service surveys in 18 states over a 25-year period up to 1955 is summarized in table 1.

Other studies indicate that, of the 10 million persons in the United States thought to have some form of rheumatism, 4,500,000 have true arthritis, with 200,000 being totally disabled and 800,000 partially disabled. Lost wages approximate 700 million dollars annually. Rheumatic fever alone, while declining in mortality from 6 per 100,000 population in 1905 to 0.3 per 100,000 in 1953, still affected 1 million persons in the United States.

Figures from the Netherlands, with a population of 11 million, indicate that rheumatism affects 15% of males and 20% of females over 15 years of age. Of the 10,000 or more affected by rheumatoid arthritis, with or without spondylitis, at least 10% were incurable invalids. Twenty per cent of all sickness benefits issued in 1953 were for rheumatic diseases.

This is the first of three installments. The second will appear in the Nov. 7 issue.

The Committee of the American Rheumatism Association consists of Drs. Darrell C. Crain, Washington, D. C., Chairman; Wallace Epstein, San Francisco; David Howell, Miami; Harry Margolis, Pittsburgh; Elbert Phelps, Washington, D. C.; William Rawls, New York; Edward Rosenberg, Chicago; J. Edwin Seegmiller, Bethesda, Md; Lawrence Shulman, Baltimore; Leon Sokoloff, Bethesda, Md; Harry Thompson, Tucson, Ariz.; and Elam Toone, Richmond, Va.

Reprints of the full text of this primer are available from the American Rheumatism Association, 10 Columbus Circle, New York 19. The price per copy is 50 cents.

Organization of the Attack on Rheumatic Diseases

During the past quarter-century medical societies devoted to the study of rheumatic diseases have been organized in most of the principal countries of the world. Of these the American Rheumatism Association continues to be numerically the largest, with over 1,200 members. In addition to national societies, international boundaries are crossed in the Pan American League Against Rheumatism, the European League Against Rheumatism, and the International League Against Rheumatism. The American Rheumatism Society holds two meetings each year. Most of the other national societies meet once a year, and the International League meets once every four years. The interest in these meetings among rheumatologists as well as nonrheumatologists emphasizes the rising tide of energies in professional fields to find causes and cures for the rheumatic diseases.

TABLE 1.—*Incidence of Various Rheumatic Diseases—Effect on Disability and Hospitalization*[*]

Rates per 1,000 Population, No.	Arthritis and Chronic Rheumatism	Rheumatic Fever	Other Diseases of Bones, Joints, and Locomotor Organs	Lumbago, Myalgia, and Myositis	Backache
Total cases	17.0	2.3	7.3	6.1	3.0
Disabled cases[†]	8.5	1.9	3.1	3.5	1.3
Bed cases[‡]	5.3	1.5	1.7	2.2	0.78
Days of disability per 1,000 population	934.0	255.5	194.0	26.1	...
Mean days of disability per case	130.5	125.1	75.3	8.3	...
Hospital admissions per 1,000 population	0.59	0.17	0.72	...	...
Hospital days per 1,000 population	4.8	36.7	40.2	...	...
Mean days per hospital admission	12.1	168.7	61.3	...	...
Mean hospital days per case	...	54.3	46.7	...	...

[*] All data calculated on basis of annual incidence.
[†] Unable to perform usual duties for one day or more.
[‡] Confined to bed more than one day.

The establishment in the United States in 1951 of the National Institute of Arthritis and Metabolic Diseases as one of the National Institutes of Health allied the resources of our federal government with those of the voluntary organizations and other interested parties in a nationwide attack on this group of afflictions. Through the research conducted in its own laboratories at Bethesda, Md., and by means of grants to nonfederal institutions, the Institute has become a major partner in this effort in a relatively brief period. The research grants program provides financial support to qualified scientists throughout the country for a wide variety of fundamental laboratory research and applied investigations necessary to continued advances in the pathogenesis, diagnosis, and treatment of these diseases as well as rehabilitation of persons afflicted with arthritis. At the same time, the institute's training grants program has been a major factor contributing to effective dissemination of knowledge and modern concepts of rheumatic diseases among medical students and physicians. Grants supporting general training in rheumatology have been awarded to almost half of the nation's medical schools, and this number can be expected to increase as additional highly trained physicians become available for academic positions. A third program, for the advanced training of outstanding persons, provides stipends for one or more years of specialized activity.

Also assisting in the attack on rheumatic diseases is the Arthritis and Rheumatism Foundation, a voluntary fund-raising health agency whose medical program (research, professional education, and medical care) is formulated and implemented by a medical and scientific committee consisting of physicians and scientists nominated to office by the American Rheumatism Association. The foundation has 53 chapters in 41 states. Among its professional activities the foundation conducts a research fellowship program which awards annually about 30 predoctorate, postdoctorate, and five-year senior investigator fellowships. The foundation publishes the *Bulletin on Rheumatic Disease,* a monthly scientific publication, which it distributes to about 45,000 physicians in every continent of the globe. The "Primer on Rheumatic Diseases" is distributed by the foundation annually to senior medical students and the "Rheumatism Reviews" to interns, residents, and fellows. In addition, the several professional educational activities of the American Rheumatism Association are supported almost entirely by the Arthritis and Rheumatism Foundation.

Classification of Rheumatic Diseases

The classification of rheumatic diseases used herein is that which has been officially adopted by both the American Rheumatism Association and the Standard Nomenclature of Diseases and Operations.

There are, of course, inherent difficulties in classifying diseases whose etiology is unknown. For this reason, differences of opinion are held on several items in this table. For example, there is good evidence, both clinical and laboratory, that rheumatoid spondylitis differs in important respects from rheumatoid arthritis, while arthritis associated with psoriasis differs from the classic variety. Many clinicians feel that these differences should be more adequately expressed in the classification. In addition, some continue to prefer the simpler "osteoarthritis" to the more descriptive "degenerative joint disease." The term "mixed arthritis" is dropping out of usage and is not included here, even though some patients may manifest both rheumatoid and degenerative joint disease. The preferable custom of diagnosing the major cause of disability, with secondary diagnosis of less important condition, is customarily used. It is open to question whether "intermittent hydrarthrosis" deserves a separate heading, or whether "fibrositis" and "myositis" can be listed as individual entities; the painful shoulder syndromes warrant more precise designation. As clearer understanding of the various diseases is obtained changes will, of course, be made. However, the benefits of a standard classification and terminology outweigh minor differences of opinion regarding form.

Rheumatic Fever

Rheumatic fever is an inflammatory process of unknown etiology, characterized by acute polyarthritis, with accompanying carditis, which may become chronic. All ages are susceptible but the greatest incidence of the disease occurs in children between 6 and 9 years of age. In the United States a definite geographical pattern is discernible, with Colorado, Utah, New York, Pennsylvania, and Massachusetts reporting the highest proportion of cases. The exact incidence of the disease is difficult to determine, since the occurrence of late chronic manifestations without recognized antecedent acute episodes indicates the existence of symptomless or atypical forms not presently understood. In countries where rheumatic fever is reportable rates vary from 11 to 30 per 10,000 persons per year. Rheumatic heart disease has been found in 1 to 4% of school children, while 7% of serial autopsies at a general hospital showed evidence of such cardiac abnormalities. Acute attacks have shown a declining rate in recent years. Although this is in part due to the widespread use of antibiotics in the treatment of patients with upper respiratory disorders, other factors such as improved nutrition and housing are of apparent significance, since the decrease had been noted prior to the advent of specific antistreptococcic therapy.

Etiology.—The etiology of rheumatic fever remains an enigma. Although acute episodes characteristically develop 10 to 20 days after upper respiratory infections due to group A beta hemolytic streptococci, organisms cannot be recovered from involved tissues or body fluids other than the pharynx, and even these are frequently not obtained after the onset of symptoms. Specific antibacterial therapy is of prophylactic value but useless as a therapeutic measure. Hypersensitivity suggested by these data lacks significant supportive evidence, as do other hypotheses of etiology. It is therefore apparent that, although infection by the beta hemolytic streptococcus initiates the disease process, the exact mechanism by which this is accomplished is unknown.

Pathology.—The lesions of rheumatic fever may be found in many organs, but the heart is the site of the most characteristic and consequential involvement. All portions of the heart may be affected. The characteristic microscopic lesion, known as the Aschoff body, is a submiliary granuloma, usually located adjacent to small myocardial vessels; however, it may occur in other cardiac and extracardiac locations. Swelling and fragmentation of collagen fibers are found in these foci as well as aggregations of characteristic large cells; these lesions heal with scar formation. The Aschoff bodies are generally regarded as pathognomonic of rheumatic activity, and it is of considerable importance that they are found in approximately 40% of auricular appendages amputated during mitral commissurotomy in clinically quiescent cases of rheumatic heart disease. Verrucous valvulitis is followed by healing with fibrous thickening and adhesion of valve commissures and chordae tendineae. This leads to variable degrees of incompetence or stenosis of the valves and resultant hypertrophy and dilatation of the heart. Subcutaneous nodules, seen during active phases of the disease, are composed of edematous, cellular granulomatous tissue. The cells involved closely resemble those of the Aschoff body, and localized areas of "fibrinoid" swelling of subcutaneous collagen bundles may occur. Unlike the subcutaneous nodules of rheumatoid arthritis little necrosis or fibrosis is seen. Synovitis is usually mild and nonspecific; however, foci comparable to subcutaneous nodules may be seen within the wall of the joint. Disseminated arteritis occurs, particularly within the lungs. The status of rheumatic pneumonia remains controversial at present.

Table 2.—*Classification of Rheumatic Diseases*

Arthritis due to infection. Specify joint and infection, when known, as:
    Arthritis of the spine due to tuberculosis
    Arthritis of the knee due to gonococcic infection
    Arthritis of the wrist due to pneumococcic infection
    Arthritis of the knee due to syphilis
Arthritis due to rheumatic fever. Record rheumatic fever as primary diagnosis invariably
Arthritis, rheumatoid, of ... Specify, as:
    Arthritis, rheumatoid, multi[illegible] atrophic arthritis, chronic infectious [illegible]
    Arthritis, rheumatoid, of spi[illegible] ankylosing spondylitis, von [illegible]dylitis ankylopoietica, spondylitis [illegible]
Arthritis due to direct trauma of ... Specify joint and trauma, as:
    Arthritis of knee due to contusion
    Arthritis of elbow due to habitual dislocation
Neurogenic arthropathy (Charcot joint). Specify joint and cause, as:
    Tabetic arthropathy of knee
Arthritis due to gout. Specify joint. Record gout as primary diagnosis invariably
Degenerative joint disease, multiple, due to unknown cause (osteoarthritis, hypertrophic arthritis, degenerative arthritis, chronic senescent arthritis)
New growths of joints. Specify joint and neoplasm, as:
    Synovioma of knee
Hydrarthrosis, intermittent of ... Specify joint
Fibrositis. Specify joint or area
Myositis, bursitis, neuritis, and neuralgia. Specify muscle, bursa, or nerve involved
Diseases in which arthritis, arthropathy, or arthralgia is frequently associated (diagnose disease, list joint manifestation as symptom):
    Acromegaly
    Acute disseminated lupus erythematosus
    Cyst of meniscus of knee
    Dermatomyositis
    Drug intoxication. Specify drug when known
    Erythema multiforme exudativum
    Erythema nodosum
    Hemophilia
    Hysteria
    Ochronosis
    Osteochondritis dissecans
    Osteochondromatosis
    Polyarteritis nodosa
    Psoriasis
    Purpura, various types
    Raynaud's disease
    Scleroderma
    Serum sickness

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* Names in parentheses are synonyms.

Clinical Features.—The classic attack of rheumatic fever appears as an acute migratory polyarthritis involving primarily the larger joints and accompanied by signs and symptoms of an acute febrile illness. In approximately one-half of the cases it is possible to elicit a history of a preceding upper respiratory infection, with an intervening latent asymptomatic period of one to three weeks' duration.

Evidence of cardiac involvement may be noted concurrent with the first arthritic symptoms or may appear shortly thereafter. These may include signs of myocarditis, pericarditis, or valvular disease (usually the mitral, less commonly the aortic valve, or involving both the mitral and the aortic), a prolonged P-R interval in the electrocardiogram, and congestive heart failure. Various skin rashes, particularly erythema marginatum, are not uncommon; subcutaneous nodules are a less frequent finding. Pleuritic, precordial, or abdominal pain may occur, with mild or absent joint symptoms, making the diagnosis difficult. Evidences of constitutional involvement include headache, lassitude, fatigue, fever, anorexia, and nausea; prostration may be present in severe cases. Patients with rheumatic heart disease may develop subacute bacterial endocarditis. Chorea minor (Sydenham's chorea) is frequently associated with juvenile rheumatic fever and may be causally related to it.

The course of the disease is subject to extreme variations. Patients with mild cases may have only a transient polyarthritis of a few days' duration; those with severe cases may run the gamut of all signs and symptoms noted above, progressing to severe toxemia, cardiac decompensation, and death within several weeks. With treatment, however, the majority will make a complete recovery within three to four months. But recurrences, in the absence of streptococcic prophylaxis, are not rare, and with each attack the possibility of permanent heart damage is increased. It has been well stated that rheumatic fever "licks the joints but bites the heart."

Laboratory Findings.—Although no specific test will establish the diagnosis, certain laboratory findings are extremely helpful. Chief among these are changes in the electrocardiogram (primarily prolongation of the P-R interval above 0.18 in children and 0.21 seconds in adults) and elevation of the serum antistreptolysin-0 titer (above 200 in most laboratories, although standards vary). Anemia, leukocytosis, elevated sedimentation rate, and positive C-reactive protein test result are also noted during the acute phase of the disease. Group A her[illegible]tic streptococci may at times be recovered r[illegible] pharynx in the early stages. As the disease [illegible] haryngeal cultures and those from other [illegible] ids are negative.

Differential Diagnosis.—Early cases of rheumatic fever may at times be confused with rheumatoid arthritis and differentiated only by adequate observation of the course of the disease over several weeks or months. Historical or serologic evidence of a preceding streptococcic throat infection suggests rheumatic fever, as does a change in the electrocardiogram. In general, the patient with acute rheumatic fever appears sicker, has a higher temperature, a greater leukocytosis, and a more dramatic response to treatment with salicylates than does the patient with rheumatoid arthritis presenting comparable joint involvement. As time goes on the arthritis subsides, leaving no residual articular damage, whereas the heart may show permanent injury. In rheumatoid arthritis, however, the opposite is the rule and the joint involvement becomes more persistent. Laboratory aids may be helpful in differentiation: In rheumatic fever the antistreptolysin titer is elevated and the agglutination titer for sensitized sheep cells and latex or bentonite particles is normal. Congenital heart disease or tuberculous pericarditis occasionally presents facets clinically compatible with rheumatic fever, but consideration of the total picture, including duration, severity, and the presence or absence of other lesions, usually aids in establishing the correct diagnosis. Fever of undetermined origin may be rheumatic. If a patient is known to have had prior rheumatic valvular disease, repeated blood cultures may be indicated, since subacute bacterial endocarditis is a possible cause of fever in a person known to be rheumatic. A picture similar to that of rheumatic fever may be presented by a group of systemic inflammatory diseases affecting similar structures in the body; these include polyarteritis nodosa, systemic lupus erythematosus, and dermatomyositis. These are rare enough to warrant preliminary consideration of rheumatic fever in the doubtful case. Such diseases may be recognized by careful study of the clinical picture, by laboratory data, or, if necessary, by biopsy of material from muscle or skin lesions. Particularly confusing is the drug sensitivity with fever and polyarthritis which may occur after penicillin administration for a previous pharyngitis. The presence of cardiac abnormalities is indicative of rheumatic fever, while pruritic rash or urticaria tends to incriminate penicillin sensitivity. The subcutaneous nodule of rheumatic fever, although found in only 10% of cases, may be considered as a specific rheumatic lesion and should be looked for periodically in doubtful cases. The abdominal pain of patients with minimal articular symptoms may be difficult to differentiate from that of a surgical abdomen. Absence of muscular rigidity and localizing signs usually are sufficient to forestall operation until other evidences of rheumatic fever become manifest.

In order to help clarify the diagnosis of rheumatic fever the American Heart Association has accepted and modified criteria usually referred to as "Jones criteria." These may be divided into "major," "minor," and "other manifestations." The finding of two major criteria or one major and two minor criteria indicates, as a rule, a high probability that rheumatic fever is present. The "other manifestations" may be used as supportive data. The criteria are not to be used as a substitute for good medical judgment but are recommended as a guide for careful study of questionable cases. The criteria are presented in table 3.

Treatment.—Treatment is directed chiefly to the prevention or suppression of carditis and its sequelae. Control of fever, cardiac pain, and polyarthritis are important not only for the comfort of the patient but also because their persistence indicates continuing activity which may heighten the possibility of cardiac damage. Joint involvement, however, does not lead to permanent arthritic damage. Bed rest is essential during the active phase, as is adequate nutrition.

A therapeutic course of penicillin should be promptly and routinely given in sufficient dosage to eliminate the possibility of any persistent hemolytic streptococcic infection. This should not be withheld even in a patient with negative throat cultures, as streptococci may be in inaccessible areas. Adequate blood levels of penicillin over a 10-day period are desirable. This may be achieved most readily by a single intramuscular injection of 1,200,000 units of benzathine penicillin. Other penicillin preparations may be used but they require multiple injections.

Both the adrenal glucocorticoids and the salicylates have potent antipyretic and anti-inflammatory action. Their relative merits and the value of either in preventing or minimizing permanent valvular scarring is still controversial, but there is evidence that both are valuable when given early and in adequate dosage. There is, however, usually no need to restrict therapy to a single agent and, when indicated by the presence of carditis, both corticoids and salicylates may be used to advantage. Either may produce undesirable collateral effects, but, as these are more frequent and potentially more serious with the adrenal steroids, their use makes closer observation of the patient necessary.

The risks of steroid therapy are discussed in more detail in the section on rheumatoid arthritis. Although the side-reactions outlined there may also be noted in patients with rheumatic fever, the relatively shorter period of administration makes their appearance less likely. A history of either peptic ulcer or psychotic tendencies weighs heavily against their use except as a lifesaving measure, but with these exceptions the drugs may be used if the usual precautions are observed.

It is, of course, impossible to specify exact dosage of medicaments in a disease as variable as rheumatic fever. However, the following general rules are useful: 1. The primary purpose of drug therapy is the prevention or minimizing of heart damage. 2. Combined salicylate and steroid therapy should be employed in the early stages, or later if there is evidence of acute cardiac involvement. 3. If the patient is seen more than two weeks after the onset of the disease, and neither pericarditis nor significant murmurs have developed, therapy with salicylates alone may be employed. However, since carditis may not be readily detectable in infants and young children, combined therapy is usually indicated.

Prednisone (or the equivalent of one of the other steroids having low sodium-retaining properties) dosage should approximate 10 to 15 mg. every six hours for two to three weeks, decreasing after that time as objective signs indicate subsidence of the inflammatory stage. The drug should not be decreased more rapidly than by 5 mg. every fourth to sixth day. The total period of steroid therapy will vary from 3 to 12 weeks, with a median of 6, depending on the severity of the presenting picture, the response to therapy, and the general reaction of the patient.

TABLE 3.—*"Jones" Criteria for Differential Diagnosis of Rheumatic Fever*

Major	Minor	Other Manifestations
Carditis	Fever	Weight loss
Polyarthritis	Arthralgia	Easy fatigability
Chorea	Prolonged P-R interval on electrocardiogram	Malaise
Subcutaneous nodules	Increased erythrocyte sedimentation, presence of C-reactive protein, or leukocytosis	Sweating
Erythema marginatum	Evidence of preceding beta hemolytic streptococcic infection	Pallor or anemia
	Previous history of rheumatic fever or presence of inactive rheumatic heart disease	Tachycardia when sleeping
		Erythema nodosum
		Precordial pain
		Abdominal pain
		Headache and vomiting

Salicylates are administered as acetylsalicylic acid or sodium salicylate (enteric-coated), 5 to 15 grains (0.3 to 1.0 Gm.) every four hours for a total daily dose approximating 2/3 grain per pound (40 mg. per 0.45 kg.) of body weight. Tinnitus may be unpleasant but is not considered dangerous; hyperventilation is an indication to decrease the dosage. The continuance of salicylate therapy for from one to four months after subsidence of clinical activity appears to decrease the possibility of "rebounds."

During the period of active disease bed rest is essential. Mobilization is begun cautiously when signs and symptoms of rheumatic activity have been absent for two to four weeks, and while salicylate medication is being continued. A return of rheumatic activity necessitates return to bedfast status. Cardiac failure at any period is treated in the customary manner with rest, salt restriction, and administration of digitalis, diuretics, and oxygen.

The erythrocyte sedimentation rate appears to be the laboratory test of greatest value in determining rheumatic activity. Other tests for inflammation may in some instances be helpful but are rarely necessary. Serial electrocardiograms are necessary in following the cardiac status.

Prevention.—Perhaps the greatest contribution to the control of rheumatic fever has been the appreciation of the role of streptococcic infection as a causative agent of the disease. Recurrent attacks of rheumatic fever may be prevented by avoiding streptococcic infections, and this can be accomplished by giving 1,200,000 units of benzathine penicillin intramuscularly once each month. Prophylaxis can also be accomplished by giving 250,000 units of penicillin orally twice daily. The intramuscular injection is usually preferred, since it insures that the proper dose is administered. All patients under the age of 18 years should receive a continuous prophylactic regimen. In those over 18 years of age the program should be continued at least five years after each attack and longer if there is frequent exposure to children or other probable sources of streptococcic infection.

The early and adequate treatment of upper respiratory tract infection of streptococcic origin appears to eliminate the possibility of a rheumatic attack. A single injection of 1,200,000 units of benzathine penicillin intramuscularly would appear to be adequate in accomplishing this result. An alternate plan is the injection of 600,000 units of procaine penicillin in aluminum monostearate every third day for three doses. In children the latter dose may be reduced to 300,000 units.

Patients with rheumatic valvular disease contemplating dental extraction or surgical procedures should be given a prophylactic dose of 1,200,000 units of benzathine penicillin intramuscularly, even if they are on the prophylactic regimen previously outlined.

Prognosis.—The prognosis of rheumatic fever is extremely variable and depends primarily on the degree of cardiac embarrassment, which in turn is related to the number and severity of attacks. Unless accompanied by other signs of cardiac decompensation, the presence of a rheumatic heart murmur does not warrant severe restriction of physical activity, school work, or childbearing but is a sign for adequate supervision of such activities. In this regard the attitude of the patient is important, and psychological crippling due to the knowledge of the existence of heart murmurs must be avoided. Cardiac enlargement, congestive heart failure, or auricular fibrillation, on the other hand, carry a poor prognosis and are signals for definite restriction of activities. However, prophylaxis, early therapy of streptococcic infections, and adequate treatment of recurrent attacks may appreciably alter the outlook of the severely affected rheumatic patient. Cardiac surgery, while beyond the scope of this primer, may be the means of adding many years to the life of the patient with formerly hopeless rheumatic fever.

Rheumatoid Arthritis

Rheumatoid arthritis is a chronic inflammatory disease of connective tissue manifested by arthritic and consitutional symptoms of varying degree, not infrequently leading to permanent joint deformities and chronic invalidism. It is a universal disease, which, although most frequent in temperate climates, is found throughout the world. It may start at any age, from infancy to advanced years, but the age at onset will be between 25 and 50 years, in 80% of cases. Women are affected three times as frequently as men. Because of the common occurrence of the disease (2.7% of persons over 14 in a recent epidemiologic survey in Pittsburgh) the economic aspects are of extreme importance. Affecting, as it is prone to do, young adults, it may seriously impair the earning power of the household provider, or so radically interfere with the activities of a young mother as to make childbearing and child-rearing a grave problem. As older persons become invalided from the disease their physical and financial care may wreak great hardships on other members of the family, as well as presenting psychological problems of major importance.

Etiology.—Rheumatoid arthritis is a disease of unknown cause. Many hypotheses of its nature have been entertained—infection, endocrine imbalance, hypersensitivity, and faulty adaptation to either physical or psychic stress, among others—but proof for any one of these is lacking at the present time. It has a slight tendency to be familial. Clinical and pathological changes, comparable to those of rheumatoid arthritis, occur in appreciable numbers of patients with other so-called collagen diseases, particularly systemic lupus erythematosus and polyarteritis nodosa. Whether these disorders are fundamentally related to each other or are coexisting separate entities has not been established.

Pathology.—Rheumatoid arthritis is invariably described as a systemic disorder. Constitutional manifestations of fever and asthenia, with laboratory evidences of inflammation, are usually present during acute stages of the diseases. Nevertheless it is the joint changes which characterize the disease, and extra-articular lesions cannot be demonstrated consistently. When present, the individual changes are for the most part lacking in diagnostic specificity.

Articular Lesions: The articular lesions vary greatly with the stage and severity of the disease. The earliest changes are recognized in the synovial tissue lining the articular cavities. They are of a nonspecific inflammatory type, including congestion, edema, exudation of fibrin and leukocytes, formation of granulation tissue, and infiltration with chronic inflammatory cells. As a result, the synovial tissue may become greatly thickened with villous hypertrophy. As the disease progresses, the peripheral portions of the articular cartilage are involved in the inflammatory reaction and undergo lysis, with replacement by granulation tissue. Comparable inflammatory changes frequently are present in the subchondral marrow spaces. The adhesive granulation tissue extending from the synovial lining across the cartilage is referred to as a pannus. As it progresses, the articular surface of the bone may be destroyed and rarefaction of the juxta-articular bone may develop. The majority of the infiltrating inflammatory cells are lymphocytes and plasma cells. They are distributed both diffusely and in focal nodular aggregates. Although these synovial changes are characteristic of rheumatoid arthritis, they may be seen in other chronic joint diseases. In addition to these nonspecific changes, focal lesions that resemble the more specific granuloma-like nodules present in the subcutaneous tissue and elsewhere may at times be found.

As the disease progresses adhesions may form between the apposing surfaces of granulation tissue. Cicatrization and metaplasia of the granulation tissue may result variously in fibrous, cartilaginous, and bony ankylosis. *Severe deformity of the joints* may arise both from inflammatory destruction of the joint surface and from involvement of the adjacent tendons.

Subcutaneous Nodules: Although seen in only 15 to 20% of cases, the subcutaneous nodules of rheumatoid arthritis demonstrate the most characteristic histological lesion of the disease. The nodules have granuloma-like features. Within the nodules three elements are recognized: a central zone of "fibrinoid" necrosis of collagenous tissue; a surrounding palisade of radially arranged, elongated connective tissue cells; and a periphery of chronically inflamed granulation and fibrous tissue. There is some evidence that inflammation of blood vessels plays a primary role in the development of these nodules. In general, they are similar to the subcutaneous nodules of rheumatic fever but show more necrosis and fibrosis. The differences have been explained on the basis of the greater duration and size of the rheumatoid lesion. On rare occasions, nodules are seen in persons not known to have rheumatoid arthritis.

Heart: Although not often apparent clinically, evidences of heart disease have been found with some frequency at autopsy in patients with rheumatoid arthritis. Pericarditis has been seen in 25 to 40% of cases. There are conflicting reports of the occurrence of valvular lesions resembling those of rheumatic fever, the figures varying from 12 to 65% of patients with rheumatoid arthritis coming to autopsy. Within recent years there has emerged a concept of specific rheumatoid heart disease characterized not only by pericarditis, myocarditis, and coronary arteritis but also by granulomatous inflammation of the heart valves, comparable to that of the subcutaneous nodules. These lesions are only infrequently of sufficient magnitude to be apparent clinically.

Arteries: Inflammation of isolated small arteries has been demonstrated in appreciable numbers of patients with peripheral rheumatoid arthritis. The arteritis has a variable character, often being mild and of limited extent. At times, however, the lesions may be associated with peripheral neuropathy or systemic polyarteritis nodosa. It has been suggested that severe vascular changes are more frequent in patients treated with large doses of steroid compounds than in untreated patients.

Miscellaneous Lesions: Focal infiltrations of lymphocytes occur in the skeletal muscles in the majority of patients with rheumatoid arthritis but cannot be regarded as pathologically specific. Atrophy of muscle fibers is common but degeneration is infrequent. Hyperplasia of lymph nodes may occur in the regions of affected joints but is occasionally generalized. The changes are nonspecific and are not to be confused with giant follicular lymphadenopathy. Chronic scleritis, at times with uveal herniation (scleromalacia perforans), *is an infrequent lesion and resembles the* subcutaneous granuloma. Nonspecific iridocyclitis occurs commonly in juvenile rheumatoid arthritis and ankylosing spondylitis and less frequently in peripheral rheumatoid arthritis. Granulomatous nodules are found infrequently in the lungs and pleura, as in other viscera. Secondary amyloidosis has been reported in approximately 20% of autopsies on patients hospitalized for rheumatoid arthritis.

Clinical Features.—Although the crippled patient with far-advanced rheumatoid arthritis presents a characteristic picture, the onset and course of the disease are subject to wide variations. Constitutional symptoms of generalized weakness, fatigue, and morning stiffness may precede the articular manifestations but are usually mentioned by the patient only in retrospect. With few exceptions, the joint symptoms form the initial complaint.

In 75 to 80% of the cases the onset is insidious. The patient may awaken one morning with one or more joints sore and stiff. As the day progresses these become moderately inflamed, with modest swelling, redness, and soreness. These symptoms may persist for several days or even several weeks. Indeed, stiffness and pain may be present before demonstrable swelling is noted, and, although swelling appears, other signs of inflammatory reaction such as redness and warmth may be lacking. Within a period varying from several days to several months other joints may become similarly involved. In the majority of cases, rheumatoid arthritis is a progressive disease and once begun does not entirely subside. Symptoms and signs in articulations involved may resolve completely, subside partially, remain undiminished, or develop acute (and often severe) exacerbations. Despite this tendency to chronicity, periods of spontaneous remission may occur during which the patient is relatively asymptomatic. Usually, however, these remissions are not complete. Further exacerbations occur and, as time progresses, various deformities may ensue.

In contrast to this mode of onset, approximately 20 to 25% of the cases are ushered in by a fulminating phase in which one or more joints abruptly become markedly swollen, painful, and tender with localized heat and inflammation. A migratory type of polyarthritis simulating rheumatic fever may then persist for several days or weeks. Some of these fulminant cases progress to severe deformities within a matter of weeks, often in spite of active therapy. Usually, however, this phase will subside after several weeks, the case then progressing to the more usual chronic course of exacerbations and remissions.

Any diarthrodial joint in the body, including the temporomandibular and sternoclavicular, may be involved. In the hands the proximal interphalangeal joints are particularly prone to be affected, and, as they enlarge, the fingers develop a characteristic fusiform appearance. The metacarpophalangeal articulations of the index and middle fingers are also peculiarly susceptible. In Army hospitals a high percentage of cases are found to start in the feet. As the disease progresses, deformities of varying degree may be encountered. Probably the most frequent are those of the hand, involvement at the metacarpophalangeal level resulting in flexion and ulnar deviation of the fingers. Volar subluxation of the carpus, imperfect extension of the elbows, and partially flexed knees are further examples of this situation. In cases of advanced disease contractures, bony ankyloses, subluxations, or dislocations of joints may occur. Muscular weakness and atrophy may be prominent.

The skin of the extremities may become smooth, glossy, and atrophic (sclerodactylia). There may be redness of the thenar and hypothenar eminences, while the hands are often cold and clammy.

When present, subcutaneous nodules are found most frequently over the extensor surface of the proximal third of the ulna, distal to the olecranon process, but they may be widespread in the region of bony prominences and in superficial tendons. They vary from scarcely palpable seed-like particles to lesions 3 to 5 cm. in diameter. Usually not painful, they may occasionally ulcerate and become secondarily infected if subjected to undue pressure. Having once appeared, they usually persist throughout the disease, although they may decrease in size and some even disappear during a lengthy remission.

Constitutional symptoms of weakness and fatigue in varying degrees are common throughout the course of the disease. In addition, during periods of acute fulminating joint involvement there is likely to be malaise, fever, and anorexia. It is, however, a matter of interest that profound joint changes may occur in healthy, robust persons.

Splenic enlargement occurs in approximately 5 to 10% of patients and may be associated with leukopenia (sometimes called Felty's syndrome). Generalized lymphadenopathy of moderate degree is commonly observed. Joint changes resembling rheumatoid arthritis occur in 4 to 5% of patients with ulcerative colitis.

One of the still unresolved riddles in this complex condition pertains to the exact delineation of the role played by emotional and psychological reactions in the etiology and course of the disease. A high percentage of patients will exhibit a passive, dependent personality, with frequent periods of hostile aggression toward family, physician, and associates. Yet this is by no means universal, and rheumatoid arthritis will be found in patients with all personality patterns. Still, the frequency with which exacerbations of the disease are related to periods of major emotional stress cannot be ignored. Further contributing to this problem is the fear reaction engendered by the victim's realization of the consequences of a chronic, potentially incapacitating disease. Thus, whether they be cause or effect or a combination of both, psychological reactions early assume a place of importance in the disease state.

Diagnosis.—Although far-advanced cases of rheumatoid arthritis are easily recognized, the protean nature of the early disease may make definite diagnosis difficult. Rheumatic fever, gout, disseminated lupus erythematosus, and osteoarthritis will cause the greatest confusion.

Rheumatic fever may simulate rheumatoid arthritis during the early acute inflammatory stages when both may present a migratory polyarthritis. The differential diagnosis is discussed above.

Although gout may cause some confusion, the acute severe monarticular self-limiting episodes usually distinguish it from the less acute polyarticular involvement of rheumatoid arthritis. The favorable therapeutic response to colchicine, so characteristic of early acute gout, does not occur in rheumatoid arthritis. Hyperuricemia aids in confirmation of the diagnosis of gout. Biopsy of synovial tissues or suspected tophi may at times be of assistance.

Systemic lupus erythematosus may be indistinguishable from rheumatoid arthritis and, indeed, it is still uncertain whether the two at times coexist or are part of the same general disease process. However, patients with lupus erythematosus usually show only minimal articular symptoms but severe constitutional manifestations with visceral involvement and the characteristic L. E. cell phenomenon.

Joint symptoms occurring in middle-aged patients may cause some difficulty in differentiation between rheumatoid arthritis and osteoarthritis. The presence of inflammatory signs usually indicates rheumatoid arthritis, although this is not always the case. Osteoarthritis is more prone to be localized to one or two joints, whereas rheumatoid arthritis involves multiple joints. In the hands, involvement of the proximal interphalangeal joints suggests rheumatoid arthritis and that of the distal interphalangeal joints, osteoarthritis. An accelerated erythrocyte sedimentation rate and serologic reactions may be of aid in diagnosis. In order to assist in the differential diagnosis, the American Rheumatism Association has adopted the following criteria for diagnosis of this disease.

Classic Rheumatoid Arthritis

The diagnosis of classic rheumatoid arthritis requires the satisfaction of seven of the following criteria. In criteria 1 through 5 the joint signs or symptoms must be continuous for at least six weeks (any one of the features listed under "Exclusions" will exclude the patient from this category).

1. Morning stiffness.
2. Pain on motion or tenderness in at least one joint (observed by a physician).
3. Swelling (soft tissue thickening or fluid, not bony overgrowth alone) in at least one joint (observed by a physician).
4. Swelling (observed by physician) of at least one other joint (intervals free of joint symptoms between the two joint involvements of not more than three months).
5. Symmetrical joint swelling (observed by a physician) with simultaneous involvement of the same joint on both sides of the body (bilateral involvement of the midphalangeal, matacarpophalangeal, or metatarsophalangeal joints is acceptable, without absolute symmetry). Terminal phalangeal joint involvement will not satisfy this criterion.
6. Subcutaneous nodules (observed by a physician) over bony prominences, on extensor surfaces, or in juxta-articular regions.
7. Roentgenographically visible changes typical of rheumatoid arthritis (which must include at least bony decalcification localized to or greatest around the involved joints and not just degenerative changes). Degenerative changes do not exclude the diagnosis of rheumatoid arthritis.
8. Positive result of agglutination test—demonstration of the "rheumatoid factor" by any method which, in two laboratories, has been positive in not over 5% of normal controls—or positive result of streptococcic agglutination test.
9. Poor mucin precipitate from synovial fluid (with shreds and cloudy solution).
10. Characteristic histological changes in synovial membrane, with three or more of the following findings: marked villous hypertrophy; proliferation of superficial synovial cells, often with palisading; marked infiltration of chronic inflammatory cells (lymphocytes or plasma cells [illegible] tendency to form "lymphoid [illegible] of compact fibrin, either on surface or interstitially; or foci of cell necrosis.
11. Characteristic histological changes in nodules showing granulomatous foci with central zones of cell necrosis, surrounded by proliferated fixed cells, and peripheral fibrosis and chronic inflammatory cell infiltration, predominantly perivascular.

Definite Rheumatoid Arthritis

The diagnosis of definite rheumatoid arthritis requires the satisfaction of five of the above criteria. In criteria 1 through 5 the joint signs or symptoms must be continuous for at least six weeks (any one of the features listed under "Exclusions" will exclude a patient from this category).

Probable Rheumatoid Arthritis

The diagnosis of probable rheumatoid arthritis requires the satisfaction of three of the above criteria. In at least one of criteria 1 through 5 the joint signs or symptoms must be continuous for at least six weeks (any one of the features listed under "Exclusions" will exclude a patient from this category).

Possible Rheumatoid Arthritis

The diagnosis of possible rheumatoid arthritis requires the satisfaction of two of the following criteria and total duration of joint symptoms must be at least three weeks (any one of the features listed under "Exclusions" will exclude a patient from this category).

1. Morning stiffness.
2. Tenderness or pain on motion (observed by a physician) with history of recurrence or persistence for three weeks.
3. History or observation of joint swelling.
4. Subcutaneous nodules (observed by a physician).
5. Elevated sedimentation rate or C-reactive protein level.
6. Iritis.

Exclusions

Any one of the following clinical features constitutes an exclusion from each of the diagnoses listed above.

1. The typical rash of disseminated lupus erythematosus (with butterfly distribution, follicle plugging, and areas of atrophy).
2. A high concentration of lupus erythematosus cells (four or more in two smears prepared from heparinized blood incubated not over two hours).

3. Histological evidence of polyarteritis nodosa, with segmental necrosis of arteries, associated with nodular leukocytic infiltration extending perivascularly and tending to include many eosinophils.

4. Weakness of neck, trunk, and pharyngeal muscles or persistent muscle swelling or dermatomyositis.

5. Definite scleroderma (not limited to the fingers).

6. A clinical picture characteristic of rheumatic fever with migratory joint involvement and evidence of endocarditis, especially if accompanied by subcutaneous nodules, erythema marginatum, or chorea (an elevated antistreptolysin titer will not rule out the diagnosis of rheumatoid arthritis).

7. A clinical picture characteristic of gouty arthritis, with acute attacks of swelling, redness, and pain in one or more joints, especially if relieved by *colchicine.*

8. Tophi.

9. A clinical picture characteristic of acute infectious arthritis of bacterial or viral origin, with an acute focus of infection or in close association with a disease of known infectious origin; chills; fever; or an acute joint involvement, usually migratory (especially if there are organisms in the joint fluid or the patient responds to antibiotic therapy).

10. Tubercle bacilli in the joints or histological evidence of joint tuberculosis.

11. A clinical picture characteristic of Reiter's syndrome, with urethritis and conjunctivitis associated with acute joint involvement, usually migratory initially.

12. A clinical picture characteristic of the shoulder-hand syndrome, with unilateral involvement of shoulder and hand and diffuse swelling of the hand followed by atrophy and contractures.

13. A clinical picture characteristic of hypertrophic pulmonary osteoarthropathy, with clubbing of fingers or hypertrophic periostitis along the shafts of long bones, or both, especially if an intrapulmonary lesion is present.

14. A clinical picture characteristic of neuroarthropathy, with condensation and destruction of bones of involved joints and associated neurological findings.

15. Homogentisic acid in the urine detectable grossly with alkalinization.

16. Histological evidence of sarcoid or a positive result of the Nickerson-Kveim test.

17. Multiple myeloma as evidenced by marked increase in plasma cells in the marrow or Bence Jones protein in the urine.

18. The characteristic skin lesions of erythema nodosum.

19. Leukemia or lymphoma, with characteristic cells in peripheral blood, marrow, or tissues.

20. Agammaglobulinemia.

Laboratory Findings.—During active stages of the disease results of the several nonspecific tests for inflammation are usually positive: elevated erythrocyte sedimentation rate, C-reactive protein, and, occasionally, mild leukocytosis. The serum in most cases of peripheral rheumatoid arthritis has the ability to agglutinate or flocculate a variety of suspended particles, hemolytic streptococci, sheep red blood cells sensitized with amboceptor (anti-sheep erythrocyte rabbit serum), and latex and bentonite suspensions, among others. These phenomena apparently depend on the presence of abnormal macroglobulins in the serum. Several serologic tests based on this reaction have a high degree of diagnostic specificity (approximately 85%). They usually give negative results in patients with ankylosing spondylitis, juvenile rheumatoid arthritis, and psoriatic arthropathy. Generally accepted positive titers are sheep cell agglutination, 1:32; bentonite flocculation, 1:32; and latex particle fixation, 1:20. These agglutination reactions may not be positive, however, during the first several weeks or months of the disease, when the differential diagnosis is most difficult.

The serum globulin concentration is elevated, at least relative to the value of serum albumin. Normocytic, hypochromic anemia, refractory to iron, is commonly present during the active phases of rheumatoid arthritis. The serum uric acid concentration is usually within normal limits, as is the antistreptolysin-O titer. The synovial fluid tends to be turbid and may clot spontaneously in vitro. Its viscosity is reduced. The fluid contains an excess of leukocytes, their number varying in proportion to the severity and acuteness of the process. During acute episodes polymorphonuclear leukocytes predominate; during more quiescent periods lymphocytes are more numerous. When acetic acid is added to the synovial fluid the normal ropy mucin clot fails to appear.

Prognosis.—Because of the dramatic appearance of the severely crippled patient with rheumatoid arthritis the gravity of the prognosis in rheumatoid arthritis is commonly exaggerated. Actually, patients with mild cases may recover spontaneously and lengthy remissions in which the disease is apparently arrested may occur even in those of many years' duration. Furthermore, with proper therapy, the more severe consequences of the disease may be lightened or entirely prevented in the majority of cases.

Treatment.—Despite the lack of specific therapeutic agents, it is usually possible to control the disease or ameliorate its manifestations. However, the natural history of the disease, with spontaneous remissions and exacerbations, and the prominent psychological factors notable throughout the disease, make evaluation of individual therapeutic modalities difficult.

It would seem most convenient to classify the various treatment methods in six general categories: (1) general measures, (2) drug therapy, (3) physical therapy, (4) steroid therapy, (5) orthopedic measures, and (6) psychotherapy.

General Measures: Since arthritis is a systemic disease for which no specific cure has been found, it follows that all those general measures which will improve the patient's health, so that his natural protective resources may function optimally, must be employed to their utmost. The first of these is rest, systemic and local. Because the disease affects the muscles the patient will fatigue easily and will therefore need more general rest than the unaffected person. During acute fulminating periods complete bed rest may be indicated. Local rest, particularly in severe exacerbations, may be accomplished by splinting. During such periods at rest precautions must be taken to prevent further muscle wasting and ankylosis of joints. Toward this end active physical therapeutic measures are indicated, as will be noted below. The occasional use of sedatives at night is justified. Closely allied with rest is the matter of exercise. Patients should be taught the value of simple setting-up exercises and deep breathing exercises to help strengthen the general muscular tone, as well as specific exercises for involved limbs.

A well-balanced diet is indicated, no individual food or vitamin having been found beneficial or detrimental. Patients should be cautioned to wear warm clothing and to protect their joints, especially in cold or rainy seasons, and to avoid undue chilling and drafts. Temporary improvement in symptoms during spa therapy would appear to be related to favorable changes in environment, coupled with judicious administration of physical therapy. Foci of infection should be removed if they impair general health.

Drug Therapy: Salicylates remain the most useful drugs in the treatment of rheumatoid arthritis. All are approximately therapeutically equal, usually cheap, readily available, and well tolerated. Aspirin—plain, coated, or buffered—is the preferred drug. One to three 5-grain (325-mg.) tablets or their equivalent may be administered two to six times per day, depending on the severity of the condition. Maximum doses to the point of mild salicylism may be required for the relief of pain. Some physicians prefer to govern the dose by estimations of the serum level of salicylate, 25 mg.% being the level usually desired.

Recently developed non-narcotic analgesics have also proved helpful as pain-relieving adjuncts to therapy. Barbiturates and other sedatives may be prescribed as indicated. Treatment with codeine and other narcotics should be assiduously avoided.

Phenylbutazone has proved to be of limited benefit as an antirheumatic agent in rheumatoid arthritis. It is administered orally, 200 to 600 mg. per day. Potentially toxic properties include depression of marrow, with resultant decrease in formed blood elements; gastrointestinal irritation, with peptic ulcer and gastrointestinal bleeding; and allergic skin reactions. Although comparatively rare, when compared to the total number of cases treated thereby, nevertheless these serious side-reactions from phenylbutazone must be borne in mind. Blood counts and urinalyses should be done after the first week of therapy and then at four-week intervals. A patient who has not shown a prompt response (within 10 to 14 days) to an adequate dose of the drug will not respond to prolonged administration, and the medicament should then be discontinued.

Antimalarial compounds, such as chloroquine phosphate and hydroxychloroquine sulfate appear to suppress rheumatic activity in some patients with rheumatoid arthritis; the former in doses of 250 to 500 mg. per day and the latter in doses of 200 to 400 mg. The beneficial effects of these drugs are slow to develop, usually being noted only after three to six weeks of therapy. However, once improvement develops it is usually sustained. Toxic reactions, such as blurring of vision, nausea, anorexia, leukopenia, or dermatitis, develop in some patients, occasionally necessitating discontinuance of the drug.

Soluble gold compounds have been found useful in the treatment of many patients with rheumatoid arthritis. Their beneficial effect appears to be attendant on suppression and even arrest of the active rheumatoid process, whereby lengthy remissions may be induced. There is, however, no reversal of established deformities. Therefore, gold compounds are most effective in the early and active stages of the disease, but remissions have been induced even in long-standing cases. The palindromic variant of rheumatoid arthritis appears particularly susceptible to the beneficial effect of chrysotherapy.

The preparations of gold which have been found most dependable are gold sodium thiosulfate, gold sodium thiomalate, and gold thioglucose. All are given by intramuscular injection, usually at weekly intervals, in doses of 25 to 50 mg. The first injection is usually of 10 mg., as a test for toxicity. Subsequent doses are increased to the maintenance level. This is then continued until one of three responses is noted: (1) toxic reactions which may require discontinuance or interruption of the drug; (2) therapeutic nonreactivity, which is felt to occur if the patient notes no improvement after approximately 10 to 12 injections; or (3) adequate therapeutic response. This will usually occur between the 8th and 15th injection, at which time the inflammatory manifestations have decreased and the sedimentation rate has shown a significant drop. The injection of gold is then given every second week, and, as improvement continues, every third and finally every fourth week. It is continued at this interval until maximum remission, with normal sedimentation rate, has been noted for at least four months. To maintain such remissions monthly or bimonthly injections may be continued indefinitely, for as long as three to five years. During this period, if there is an exacerbation of symptoms, weekly injections are reinstituted according to the former program. The drug therapy is discontinued when the joints have been asymptomatic and the sedimentation rate normal for six months.

Unfortunately, serious reactions to gold may occur at any time during its administration; the appearance of these is a signal to limit or discontinue the treatment. These include dermatitis (the most common), blood dyscrasias, stomatitis, hepatitis, colitis, and hematuria. Prior to the institution of therapy each patient should be cautioned that such reactions may occur and should be told to advise the physician of the appearance of any skin rash. A small percentage of patients will note a flare-up of the arthritic process 24 to 48 hours after the administration of gold. This may usually be overcome by decreasing the size of the dose and concurrently administering antihistaminic drugs. Weekly estimations of the hemoglobin or hematocrit level, a white blood cell count, and a check of the urine for albumin should be done during the early stages of gold administration and at least once a month as it is continued. The appearance of any rash or significant blood or urine alteration during the administration is a signal to lower the dose or discontinue therapy. British anti-lewisite (BAL) has been helpful in instances of severe reaction, but undesirable effects may accompany the use of this compound, too. Corticosteroids or corticotropin are reliable and effective in controlling many of the undesirable reactions.

The acute inflammatory phase of rheumatoid arthritis may at times be controlled by the intravenous administration of either nitrogen mustard or typhoid vaccine. Remissions induced thereby are temporary, necessitating additional "follow-up" therapy with use of other modalities.

Physical Therapy: Physical therapy is of value in all stages of rheumatoid arthritis. During acute episodes local applications of warm moist compresses will assist in relieving inflammation and alleviating pain. These are also useful preceding periods of passive exercise.

In treating patients with more chronic cases a comprehensive program should be outlined by the physician (preferably a physiatrist). This may frequently be carried on by the patient at his home, with progress noted at specified intervals in the physician's office. The program will include one or two daily periods of active exercise, usually preceded by applications of heat in the form of infrared radiation. Exercises prescribed should include general ones designed to maintain proper posture and weight-bearing alignment as well as local ones to strengthen muscles and prevent or correct deformities. It is usually advisable from time to time to supplement this home program with professional physical therapy. On these occasions more active measures such as muscle massage, resistive exercises, and gentle muscle stretching may be indicated. Care must be observed to avoid forcing joints beyond their limit and thereby reactivating a latent process.

Steroid Therapy: Although corticosteroids do not basically alter the fundamental pathological process in rheumatoid arthritis, their judicious therapeutic use may be of material assistance in the management of patients resistant to other modes of therapy. The administration of adequate amounts of these hormones to patients with active rheumatoid arthritis results in dramatic alleviation of symptoms and signs, with prompt relief of pain and stiffness, reduction of fever, and reversal of certain abnormal laboratory findings (lowering of erythrocyte sedimentation rate, increase in serum albumin and decrease in serum globulin levels, improvement in anemia, and correction of synovial fluid abnormalities). The remarkable psychological improvement which many patients experience when first receiving these agents is noteworthy. This is often of considerable importance in easing the problem of nursing care and assisting in more effective acceptance of physical therapy and other general measures in management. Since the action of these drugs is one of suppression of inflammatory reactions rather than eradication of the basic causative mechanism, these benefits persist only as long as an adequate dose of the hormone is maintained and there is no increased tendency to natural remission of the disease process itself. It is therefore apparent that, if these are used in treatment of rheumatoid arthritis, administration over protracted periods of time will be necessary.

The chief difficulty attendant on the continued use of high doses of steroids pertains to those metabolic activities which eventually lead to a series of untoward side-effects resembling adrenocortical hyperfunction (Cushing's syndrome). These vary from the minor annoyances of moonface, acne, hirsutism, euphoria, fat deposition, weight gain, dyspepsia, and sleeplessness to the major complications of peptic ulcer, osteoporosis and pathological fractures, edema due to sodium and water retention, frank psychosis, hypopotassemia and muscle weakness, hypertension, glycosuria and hyperglycemia, ecchymosis, and the reactivation of such latent infections as tuberculosis. Although these are apparently rare, the use of steroid therapy in patients with rheumatoid arthritis may be associated with an increased incidence of necrotizing angiitis and peripheral neuropathy. Furthermore, continued use of steroids leads to temporary atrophy of the patient's own adrenal cortex, and apparently to certain portions of the pituitary gland also. It is therefore imperative to increase the steroid dosage when the patient is subjected to additional stress, as when undergoing surgery. Since 10 to 12 months may be required for complete restoration of adrenal function after the cessation of steroid therapy, such administration of supplemental hormones during episodes of stress may be required in this period.

In action and side-effects all the synthetic hormones are remarkably similar to their natural precursors, but when used in comparable therapeutic doses they have less tendency to promote retention of sodium and water. Accordingly their use is less frequently marred by the development of peripheral edema and hypertension. However, abdominal bloating, peptic ulcer, and increased capillary fragility, with ecchymotic areas of the extremities, are more common with these than with cortisone. All the adverse reactions noted are related to the size of the dose administered and the length of time it is continued. There is, however, a marked variation from patient to patient, and many can tolerate considerably higher doses over longer periods of time than their less fortunate co-sufferers. Much attention continues to be given to further modification of chemical structure, in an attempt to produce an "ideal steroid," and it seems reasonable to assume that one may be developed which will have antiphlogistic powers, without other metabolic effects.

Steroid therapy should therefore be reserved for those patients in whom the rheumatoid process is showing continuing activity despite an adequate trial on the simpler programs of management previously outlined in this primer. The coexistence of certain other conditions, such as active tuberculosis or other systemic infections, severe diabetes mellitus, peptic ulcer, and advanced hypertensive vascular disease, must serve as relative contraindications to their use, although in some instances appropriate therapy for these complications will permit steroid therapy to proceed without untoward incident.

The formidable risk of adverse reactions has served to limit attempts to achieve a complete suppressive effect through the administration of large doses; rather, it seems wise to regulate the daily dose to that level which will permit the patient some relief of pain and a corresponding increase in physical activities and to maintain this level over as long a period of time as possible. This can usually be obtained by the administration of approximately 37.5 to 50 mg. of cortisone per day or its equivalent in one of the synthetic hormones (10 to 12 mg. of prednisone or prednisolone, 6 to 10 mg. of triamcinolone or methylprednisolone, or 0.75 to 1.5 mg of dexamethasone). Alterations in the daily dose are accomplished extremely slowly (an increase or decrease of 2.5 to 5 mg. of cortisone or its equivalent every third to fifth day), because more rapid withdrawals may precipitate severe exacerbations of the disease. The concurrent administration of adequate doses of salicylates will usually assist in maintaining clinical control.

The local (intra-articular) injection of hydrocortisone or other steroids continues to prove useful in those patients with rheumatoid arthritis in whom active disease is confined to one or two joints or in whom involvement of a single joint is so disproportionately severe as to limit the effectiveness of the entire treatment program. Virtually any of the peripheral articulations may be injected, provided the physician is properly acquainted with the anatomic landmarks involved. Injections may be given two or three times a week during severe inflammatory periods and decreased as joint improvement occurs. With repeated injections the risk of joint infection is increased.

Orthopedic Measures: Application of splints and surgical procedures are of value in managing specific aspects of this disease. The immobilization provided by a light splint will aid in relieving the severe pain of an acutely inflamed joint as well as promote subsidence of the inflammatory reaction. However, to avoid the formation of adhesions within the joint, the splint should be removed daily, with the joint then passively carried through range-of-motion exercises. Splints are also useful for the prevention and correction of joint deformities. Those made of light aluminum are especially valuable for the hands, but for other joints deep "gutter" splints of plaster are preferable. These are generally worn all night but during only part of each day, in order to prevent the complications of disuse. When flexion contractures have occurred, plaster casts made in increasing extension combined with physical therapy may help to correct the contracture. Although the above measures will usually maintain joint function, if they fail and ankylosis appears inevitable the affected joint should be maintained in a position for optimal use. The knee should be kept extended to 180 degrees; the hip in slightly flexed position; the wrist in middorsal flexion, halfway between pronation and supination; and the elbow flexed at 90 degrees. Although prevention of deformities through the above measures is of the utmost importance, when deformities due to ankylosis or contractures have occurred selected patients may benefit from surgical correction of the deformity after the activity of the disease has subsided.

Psychotherapy: In view of the psychological factors previously mentioned it is apparent that a successful program of therapy must include consideration of the patient's personality pattern. This can usually be accomplished through sympathetic but firm management on the part of the attending physician; only rarely will formal psychiatric assistance be indicated. Even then it may not be possible, for the patient may reject the suggestion of a psychic component in his illness, laying the blame for obvious emotional outbursts on the disease rather than on his own inadequacies.

The physician must therefore impart to the patient a sense of ultimate security, acting as the crutch to be leaned on in time of need or the alter ego to be railed at in times of despair. Sympathetic attention to the patient's complaints during the initial and subsequent interviews may not only uncover underlying hostilities amenable to correction but may foster a feeling of confidence in the physician's interest as well as his abilities. The need for, and rationale of, prescribed modalities must be carefully outlined so as to insure continuity of the program. Eventually, the patient's appreciation of his own part in the entire regimen may become the greatest single factor in his improvement.

Summary of Therapy.—Because of the marked variability of the disease pattern and the lack of specific therapeutic agents, a dogmatic attitude cannot be assumed toward therapy. However, the gratifying results to be achieved by a comprehensive regimen justify an optimistic approach to the care of the patient with rheumatoid arthritis.

A conservative regimen, including adequate doses of salicylates, physical therapy, and the "general measures" previously outlined, will be sufficient to control cases of mild and moderate severity.

Continuing rheumatic activity in spite of such a program is an indication for additional measures. If this activity is not great, treatment with phenylbutazone or chloroquine may bring about control. Patients with more severe cases will probably require treatment with gold. During periods of acute fulminating activity intravenous administration of typhoid vaccine or nitrogen mustard may be helpful. Patients whose conditions show progressive deterioration in spite of these measures should be judiciously treated with steroids.

It is thus evident that the therapeutic regimen may be altered as the disease state changes. It seems wise to acquaint the patient with this eventuality during early interviews so as to forestall later doubts about the adequacy of the program. Regardless of the apparent status of the condition at any particular time, regular examinations are indicated, with frequent counseling.

The concept of rehabilitation in rheumatoid arthritis must embrace all phases of the patient's therapeutic program, including discussion with the family of adjustment of the daily work load. In mild cases this may mean only the giving up of certain minor activities so as to find time for the rest and exercise period. In others, it may mean locating work for a previously inactive patient so as to impart new interest and sense of worth. In still others, it may mean installation in home or office of devices to assist the arthritic cripple in caring for himself as much as possible. Constantly to be borne in mind is the fact that the ultimate objective of therapy is not only to control the disease process but also to make the sufferer a self-respecting and useful member of society.

Rheumatoid Arthritis of the Spine

Synonyms for rheumatoid arthritis of the spine include ankylosing spondylitis, rheumatoid spondylitis, Marie-Strümpell disease, pelvospondylitis ossificans, spondylitis ankylopoietica, and spondylitis rhizomelique. Ankylosing spondylitis is a chronic inflammatory disease of the joints of the axial skeleton, manifested clinically by progressive stiffening of the spine and pain of varying degree. Because the earliest pathological change is synovitis of the axial diarthroses, comparable to that seen in the appendicular joints in rheumatoid arthritis, the American Rheumatism Association has classified this condition as rheumatoid arthritis of the spine. There are, however, significant differences from peripheral rheumatoid arthritis and because of these many rheumatologists regard it as a separate entity. This accounts for the many names by which the disease has been known.

Etiology.—The cause of the disease is unknown. Although it is frequently suspected, infection has not been proved. It is influenced by age and sex factors, occurring 10 times as commonly in men as in women and having its onset almost invariably before the age of 50 years.

Pathology.—Two apparently separate pathological processes distinguish this form of arthritis. The first of these is a synovitis of the spinal diarthroses similar to that described in the section on peripheral rheumatoid arthritis. In the majority of cases this occurs first in the sacroiliac joints and progresses to the apophysial joints (articulating facets) of the lumbar spine and thence to the thoracic and finally to the cervical spine. As the thoracic spine is attacked the costovertebral and costotransverse articulations are also affected. The degree of involvement of the various joints shows a wide range of variations; in the sacroiliac joints complete obliteration is common, and some apophysial joints may be spared entirely.

The second pathological change involves the intervertebral fibrocartilages, in which the annulus fibrosis becomes gradually ossified, fusing the vertebral bodies into a rigid unit. The subcutaneous nodules of rheumatoid arthritis are not seen in ankylosing spondylitis unless peripheral rheumatoid arthritis is also present. Insufficiency of the aortic valve has recently been recognized as an infrequent but specific lesion of ankylosing spondylitis. It is characterized by destruction of the media of the root of the aorta and consequent separation of the commissures of the valve.

Clinical Course.—At least three-fourths of the cases start in the sacroiliac joints, with pain first identified in the lower part of the spine. As the disease progresses cephalad, the discomfort is noted at increasingly higher levels. Approximately 75% of the cases start gradually, with pain and stiffness coming on so insidiously that the patient may have difficulty later recounting the exact time of onset. Recurring sciatica is the initial complaint in approximately 10%, while the remaining 15% appear as an acute disease with an abrupt onset. This is characterized by generalized symptoms of weakness, fever, malaise, and weight loss and local symptoms of severe pain, tenderness, and stiffness usually involving the entire thoracic and lumbar spine. Such cases may pursue a rather rapid downhill course, with increasing general incapacity. In others the acute exacerbation may be aborted, and the case may then progress to a chronic course similar to those of insidious onset. Remissions and exacerbations are common. Arrest of the disease, either spontaneously or coincidentally with therapy, may occur at any time, or the disease may progress until it has involved the entire spine with ankylosis and deformity. Radicular symptoms may occur. When the disease affects the lower part of the spine, sciatica may be a manifestation of such a condition, whereas involvement of the spine at higher levels may give rise to symptoms simulating involvement of abdominal and thoracic viscera.

The most common physical finding in rheumatoid spondylitis is the rigidity of the spine. In the early cases this is noted only in the lumbar region; as the disease progresses it may involve the entire spine. Limitation of chest expansion, due to involvement of the costotransverse and costovertebral articulations, may occur early in the disease. In the lumbar spine the loss of the normal lumbar curve is frequently noted, while in the thoracic spine increase in upper thoracic kyphosis is common. When the cervical spine is involved the normal head motions are limited and the patient finds it necessary to rotate his entire body from the hips and to look out of the corner of his eyes in order to see from side to side. In the acute stages there is pain on pressure over the affected areas and muscle spasm on standing. Despite marked involvement of the spine, however, many patients retain general robust health. In others, usually those who have suffered frequent acute exacerbations, there is generalized weight loss and muscular wasting. Acute inflammatory reaction in the peripheral joints occurs in 50 to 60% of cases of rheumatoid spondylitis at some time during the disease. In at least one-half of these the peripheral symptoms are transitory and self-limiting, leaving approximately 25 to 30% of patients with rheumatoid spondylitis showing permanent peripheral involvement, most commonly of the hips and shoulders. Ocular involvement including iritis, uveitis, and iridocyclitis may occur, usually in recurring attacks; blindness may ensue from these.

Laboratory Tests.—The only laboratory procedure which is of value in the diagnosis of rheumatoid spondylitis is roentgenologic examination. Even this may be entirely noncontributory until after the patient has had symptoms of the disease for from several months to one or two years. The earliest changes are those of sclerosis in the margins of the sacroiliac articulations, followed by a haziness in which the joint loses definition when viewed in the anteroposterior projection. Complete obliteration of the sacroiliac joints may occur late in the disease. As the disease progresses, sclerosis, narrowing, and obliteration of the apophysial joints occurs, and osteoporosis of the entire spine of varying degrees is noted. Ossification of the marginal portions of the annulus fibrosus, giving the appearance known as "bamboo spine," is a late but characteristic change. The sedimentation rate and C-reactive protein level may be elevated during acute exacerbations, but do not consistently parallel the activity of the disease as measured by progression of spinal stiffening. The serologic tests give negative results.

TABLE 4.—*Significant Differences Between Rheumatoid Arthritis and Ankylosing Spondylitis*

	Rheumatoid Arthritis	Ankylosing Spondylitis
Sex ratio, males to females ..	1:4	10:1
Onset after age of 50 years ..	Frequent	Rare
Results of serologic tests for rheumatoid arthritis	+	—
Ocular manifestations	Rare	Common
Subcutaneous nodules	15%	Not present
Cardiac involvement, if present	Mitral valve, rare	Aortic valve
Therapeutic response to gold	+	—
Response to roentgenologic therapy	—	+
Ossification of annulus fibrosus	No comparable change	+

Diagnosis.—In its early stages ankylosing spondylitis of insidious onset may be confused with lumbago or low back strain. Spinal rigidity noted on attempted forward bending usually suggests a true arthritis, but a presumptive diagnosis only may be possible prior to positive roentgenologic findings. In cases of more fulminating onset with sciatic pain the differential diagnosis from a ruptured intervertebral disk may be a problem. Careful examination while the patient is in the prone position will usually reveal tenderness over the sacroiliac joints in arthritis and over the disk when this is ruptured. If spondylitis starts in the thoracic or cervical spine, the initial complaint may be referred to a viscus and may cause confusion with coronary artery disease or cholecystitis. The absence of other signs of visceral disease and the localization of tenderness in the spine usually clarify the problem.

Although involvement of the apophysial articulations of the cervical spine may be seen as a late manifestation of peripheral rheumatoid arthritis, the characteristic "bamboo spine" and sacroiliac involvement of ankylosing spondylitis are not seen. Neoplasms and tuberculosis of the spine may cause difficulty in the early stages. The sharp localization of these conditions and the severe pain accompanying malignancies usually suggest the differentiation —which is proved by roentgenologic examination.

Treatment.—No specific therapeutic modality exists. Therefore, the most important single fact the patient must learn is that this disease cannot be cured and that his future mobility depends on diligent attention to general rules of health and strict observance of daily periods of properly graded exercises. These are designed to maintain motions in the spine, preserve thoracic expansion, and promote proper weight-bearing alignment. Exercises should be preceded by a period of local application of heat to enhance circulation.

In general, mechanical supports are to be avoided. However, they may be of use in some patients with spondylitis who must continue work requiring long periods of continuous standing or sitting. During acute exacerbations and in cases of fulminating onset, bed rest is desirable. There, proper posture must be maintained, with the mattress firm and pillows avoided. Moist compresses or steam packs may be helpful in alleviating pain. As in other rheumatic diseases, salicylates are of value in relieving pain and may be employed to full therapeutic doses.

Roentgenologic therapy is often of value in controlling the acute symptoms of pain and stiffness during exacerbations. There is, however, accumulating evidence to indicate that patients so treated may be susceptible to leukemia in later life. In young girls menstrual abnormalities, including sterility, may be produced. Roentgenologic therapy should therefore be used with caution. Although its use in severe cases may be justified, the lowest possible dose should be employed.

Phenylbutazone therapy has proved its usefulness in this disease in both the acute and the chronic stage; however, because of the possibility of complications it, too, must be carefully controlled. Steroid therapy would seem to have less usefulness than it does in peripheral rheumatoid arthritis but may in some instances be of value in relieving acute exacerbations.

Summary.—As noted earlier in this section ankylosing spondylitis, although currently classified under rheumatoid arthritis, demonstrates significant differences from that disease. These are summarized in table 4.

SIMPLE OR RADICAL MASTECTOMY?—Since even in the most skillful hands the conventional radical mastectomy may cause disfigurement, dysfunction and considerable psychic morbidity, it is extremely important to determine whether it is necessary to employ it routinely or to employ it at all. To date there is no proof that the results of radical mastectomy are better than those of simple mastectomy. Pathologists may theorize on the rationale of eradicating cancer by extended surgery, but in the final analysis it is the survival of patients that counts. . . . Today, many surgeons . . . know that radical mastectomy is not the operation of choice for cancer of the breast. . . . The lymphatic drainage of the breast is so rich and replete with plexuses that the direction of spread of malignant cells through these channels is understandably unpredictable and fortuitous. Drainage is generally toward the skin surface where a subcutaneous plexus of lymphatic vessels permits the cells to be carried in almost any direction. The cells may migrate medially to the internal mammary nodes, laterally to the axillary nodes, or even to the inguinal nodes. These migrations may require months or years. Periods of quiescence are followed by fresh migrations. . . . Paths of dissemination are never predictable. The lesion can spread to the supraclavicular nodes without involving the axilla; it may spread directly into the internal mammary group and mediastinum without involving the axilla; it can extend directly into the chest, over to the other breast and axilla, into the abdomen, and even down into the inguinal nodes. . . . Unless all these possible areas for dissemination of the disease are eradicated, any procedure may be doomed to failure. . . . Proliferation along lymph channels is not the only method of dissemination. What is even more treacherous, is the spread of the disease by venous channels. . . . Surgery is the best modality of therapy for operable cancer of the breast, and simple mastectomy with postoperative radiation is to be preferred to radical mastectomy.—T. C. Case, M.D., Simple Surgical Therapy for Operable Carcinoma of the Mammary Gland, *Journal of the American Geriatrics Society,* May, 1959.

COUNCIL ON FOODS AND NUTRITION

Introduction

The Council on Foods and Nutrition has invited one of the leading authorities in the field of radiation biology to present a brief report on radioactive residues in foods. As more data are becoming available all the time, follow-up reports on the various aspects of the problem will be published in this column to keep physicians informed of current developments. The Council has authorized publication of the following report.

PHILIP L. WHITE, Sc.D., *Secretary.*

RADIOACTIVITY IN FOODS

Cyril L. Comar, Ph.D., Ithaca, N. Y.

There is little doubt that atomic energy will assume an important role in our civilization, and it is appropriate that future possible hazards should be evaluated. At the present time, it can be concluded that there is no reason for any change in our nutritional habits or food technology as a result of fall-out contamination. Research must continue, however, so that recommendations can be made to minimize the intake of radioactive contamination should this ever become necessary.

Although environmental contamination now existing is due almost entirely to fall-out from nuclear weapons, peacetime operations may become increasingly important as sources of radioactive contamination. In addition to fall-out, small quantities of radioactive materials may be released into the environment as a result of such operations as mining of uranium and thorium ore and fuel processing; reactor installations in power plants, submarines, ships, and aircraft (normal operations and accidents); and radioisotope applications in medicine, industry, and agriculture.

Determining Factors in Hazard of Radioisotopes

The relative hazard of radioactive materials will be governed by the amount released into the environment, physical half life, efficiency of transfer through the food chain to the human diet, degree of absorption by the body, and length of time retained in the body. By these criteria, the radioisotopes from fall-out of the greatest concern are iodine, barium, strontium, and cesium. Extensive data are available on the passage of these radioactive materials through food chains and subsequent implications.[1] Table 1 summarizes their characteristics from the standpoint of environmental contamination.

The radioisotopes of iodine collect in the thyroid gland and those of barium concentrate in bone. Since isotopes of both of these elements have short physical half lives, they can be dangerous only during certain periods, depending on the frequency and the nature of production of contamination. Experience has indicated that iodine-131 transmitted in milk may be important at short times after releases such as in reactor accidents. Strontium-89, which is produced in higher activities than strontium-90, may be more hazardous shortly after production, while strontium-90, with a much longer half life, becomes more dominant with time. The strontium radioisotopes, of course, are cumulative in bone. Cesium-137, which follows potassium in metabolism, is considered less of a hazard than strontium-90 because it is turned over relatively rapidly in the body, it is not selectively concentrated in any one part of the body, and it does not pass appreciably from soil to plant in the food chain.

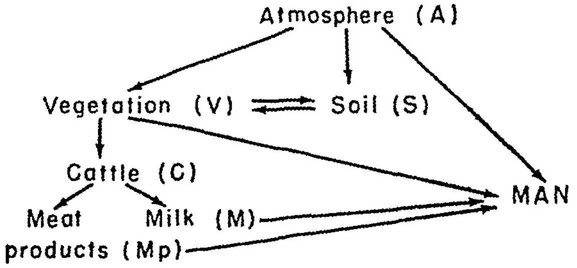

Diagram of main terrestrial food chains by means of which environmental radioactive contaminants reach the human population.

Radioactive contaminants are transferred to man by means of specific pathways through the main terrestrial food chains. These food chains are illustrated diagrammatically in the figure and the primary pathways of barium, iodine, strontium, and cesium are shown in table 1. As an example, strontium-90 is deposited from the atmosphere on the foliage of plants and on the soil. Transfer between soil and plant proceeds in both directions by normal root uptake and by washing from leaves or death

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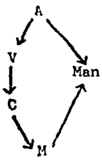
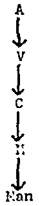
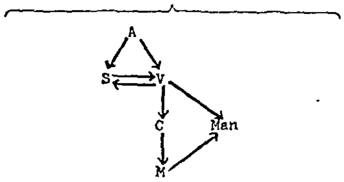
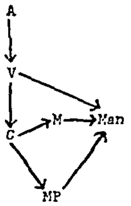
Director of the Laboratory of Radiation Biology, Department of Physiology, New York State Veterinary College, Cornell University.

of leaves. Strontium-90 reaches the human body by direct consumption of vegetation and of milk from animals that have fed on the vegetation.

The relative importance of the various pathways depends on many factors, for example, the composition of the soil (calcium level) and the nature of plant cover. A heavy root mat will tend to trap fall-out strontium and delay its reaching the soil for dilution with soil calcium, while at the same time permitting absorption into the plant from the base of the stem. The agricultural management of crops and livestock, which includes the plowing depth, fertilizer practice, and type of feeding (barn or pasture) employed, is another factor to be considered. Also of great importance are dietary habits of the population and food technology. As an illustration, in the processing of frozen vegetables, washing them prior to freezing will remove some of the surface contamination. If nuclear tests are stopped, the soil reservoir will become increasingly important; therefore, the time pattern of contamination has to be taken into account. Although food-chain considerations are extremely complex, certain generalizations can be made. It is obvious that the pathways that require considerable time in passage to man (for example, via the soil) are of no significance for the short-lived radioisotopes,[2] iodine-131 and barium-140. It also appears that the present contamination of diets originates mainly from surface contamination rather than from the soil reservoir.

TABLE 1.—*Comparison of Radioisotopes in Environmental Contamination*

	Iodine-131	Barium-140	Strontium-89	Strontium-90	Cesium-137
Physical half life	8 days	13 days	51 days	28 years	30 years
Metabolic behavior	collects in thyroid	like calcium, collects in bone	like calcium, collects in bone	like calcium, collects in bone	like potassium, collects in muscle
Removal rate from body	fast	slow	slow	slow	relatively fast
Main pathways in food chain*					
Samples for monitoring radioisotope levels	*vegetation, milk, and thyroid*	*vegetation and milk*	*soil, vegetation, milk dairy products, bone, and aquatic food*	*soil, vegetation, milk dairy products, bone, and aquatic food*	*vegetation, milk, dairy products, meat, and whole body*
Maximum permissible radioisotope concentrations, $\mu\mu c$ per liter†	3,000	200,000	7,000	80	150,000
Radioisotopes in milk, $\mu\mu c$ per liter‡	121	42	52	6.4	57
Comparative radiation dose to humans, rad	<0.04 to thyroid in 1955 and 1956	<10% of strontium-89 dose	approximately from 1 to 20% of strontium-90 dose	approximately 0.2 to 0.4 to skeleton over 70-yr. period from present tests§	approximately 0.001 per year from present levels

* A = atmosphere V = vegetation M = milk S = soil C = cattle MP = meat products.

m permissible concentrations for specific radioisotopes in drinking water as derived from recommendations of National

C rotection and Measurements. These concentrations and milk values are quoted by Public Health Service.

States from July, 1957, to July, 1958.

es recent analytical data and concepts of nonuniform stratospheric inventories developed at May, 1959, congressional subcommittee hearings.

The movement of strontium radioisotopes from soil to man is interrelated and, to some extent, governed by the simultaneous movement of calcium. In all steps of the food chain from vegetation to human bone, calcium is preferentially utilized relative to strontium. Thus, it has been calculated that at equilibrium the strontium-calcium ratio in bones of young infants would be from 3 to 12% of that in vegetation, with values of 8 to 16% in the bones of persons over 6 months of age. Although milk is our primary source of calcium, the discrimination against strontium relative to calcium in passage from the feed of the cow to its milk tends to reduce the importance of milk as a source of strontium-90. While dairy products furnish some 80% of our dietary calcium, they may supply somewhat less than 40% of the total strontium-90 intake when steady-state conditions are established. Attention should also be given to contaminated water supplies as a possible source of strontium-90. In making estimations, the entire strontium-90 and calcium intake of the population must be considered.

The soil reservoir probably will not be an important factor for cesium-137 because of the fixation of this element in the soil and its consequent unavailability to the plant. At the present time, about 60% of the cesium-137 content of the average diet is derived from dairy products, 25% from meat products, and the remainder from vegetables, cereals, and fruits.

Radioisotope Levels

The present levels of these radioisotopes in the biosphere (soil-plants-animal products–man) can be determined with reasonable accuracy by radiochemical analysis. For purposes of illustration, table

1 presents some of the average radioisotope values for milk in the United States for the years 1957 and 1958. In the early part of 1959, values for strontium-90 in milk from various locations in the United States all averaged well under 30 micromicrocuries ($\mu\mu$c) per liter. These values are below the recommended maximum permissible limits for lifetime exposure to specific radioisotopes in water. Discussion of maximum permissible levels is beyond the scope of this paper. It is urged, however, that scientists and laymen should develop a clear understanding of what is implied by figures given as maximum permissible levels and how these figures are derived.[1]

Dietary levels of strontium-90, which are expressed as micromicrocuries of strontium-90 per gram of calcium, have been estimated at approximately 0.4, 2, 4, 5, and 7 for each year from 1953 to 1957 respectively. It is estimated that the maximum levels from tests to date will occur from 1962 to 1965 and that the average maximum level in the diet of persons living in the United States at that time may reach about 24 $\mu\mu$c of strontium-90 per gram of calcium. Recent considerations indicate that much of the present strontium-90 in milk may not have come through the soil but found its way into the plant by foliar absorption or other processes. This has important implications: (*a*) if there is no further testing, the levels may fall fairly rapidly, (*b*) the contamination of food when only the soil route is operative should be much lower than at present, and (*c*) this would explain why levels in non-milk foods are not greatly lower than in milk foods as is expected because of the dairy cow's preferential use of calcium.

Milk from numerous areas has been analyzed to determine the local variation in dietary levels of strontium-90. The highest values observed were about five times the mean value, while milk from cows fed on vegetation grown in low-calcium soils were approximately twice the mean value. There appears to be less variation in the levels found in the human population, presumably because the individual consumes food that originates from many areas. It is not yet possible, however, to express variability in precise statistical terms.

The most direct and important evidence comes from analysis of tissue samples from the human population. Typical values, calculated and expressed in terms of radiation dosage rather than concentration of radioisotopes, are given in table 1. A scale of values to indicate expected response of man to radiation is presented in table 2. It can be noted that present and anticipated levels of radioactivity in man, based on the effects of nuclear tests to date, are below those known to produce any observable effects. However, indiscriminate testing of nuclear weapons, either by many nations or at higher rates, could lead to levels of strontium-90 in the food chain that would be of definite concern. The most difficult issue, particularly because of its moral overtones, is whether present levels (also of carbon-14) [3] will produce absolutely no incidence or will produce only finite incidences of genetic or somatic harm in the world population. This is a complex and controversial matter relating to linearity of response and patterns of threshold versus non-threshold behavior at low levels.

Low-level monitoring, which detects excess radiation before health hazard levels are reached, will become important as a public health function to give advance warning of any peacetime operational difficulties. Public reassurance will be provided by monitoring at natural radiation levels before and after nuclear installations are placed in operation.

Summary

Although at the present time there is no indication for a change in our dietary habits, broad-scale research on the problem of radioactivity in foods and its implications must continue for future public welfare. Even if testing of nuclear weapons is halted, peacetime applications of atomic energy will release some radioactive materials into the environment. Therefore, close supervision of the dietary levels of radioisotopes and understanding of possible effects on man are necessary for evaluation of atomic energy benefits versus biological cost.

TABLE 2.—*Effects of Radiation on Man*

Radiation Dose, rad	Source and Conditions	Observations
3,000-6,000	3.6 μc radium or x-radiation to skeleton	Bone sarcoma
300	0.4 μc radium	Minimal nondeleterious bone changes
90	0.1 μc radium	No observable effects
50-60	(suggested as levels that would double leukemia incidence)	
7-15	Natural background	No observable effects
10	(recommended upper limit of radiation from any man-made source)	
0.2-0.4	(estimated dosage from strontium-90 from tests *to time of writing*)	
0.05	(estimated dosage from cesium-137 from tests to time of writing)	

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HARRIS'S MIGRAINE OR CLUSTER HEADACHES

MIGRAINE is a fascinating disorder, kaleidoscopic in its manifestations and instructive in the leads it affords about function of the brain and about behavior. Despite a statistical relation between migraine and epilepsy, the sufferer of migraine has within him something that powerfully resists the spread of the abnormal electrical discharge. Otherwise why does he not have convulsions, when he is subject to all sorts of other jacksonian phenomena. Perhaps the abnormal electrical activity during the prodromata of migraine is essentially cortical and does not spread far from its original focus. Attacks that produce involuntary movement of a skeletal muscle are rare; weakness or inefficiency occur to be sure—and numbness, dysphasia, and of course the marvelous spectrum of scintillating scotomata.

A variant of the galaxy that is migraine was recently reported by Bickerstaff[1] under the heading "The periodic migrainous neuralgia of Wilfred Harris." This condition[2] was first systematically described by Harris in 1926. A decade later when he termed it ciliary neuralgia, Harris weakened his original title and sent many practitioners on a trek through the sinuses and nerve plexuses with probe and scalpel. This type of headache has been known also by Horton's[3] term, histaminic cephalalgia. The groups at Duke[4] and at the Montefiore Hospital in New York[5] have called it "cluster headache," because of the curious tendency of attacks to occur in clusters between periods of freedom.

Despite the fact that the syndrome is rarely recognized when first seen, it is characteristic. The patient is more often a man than a woman (between two and four to one) and between the ages of 30 and 50 years. Bickerstaff reported a case in a patient 11 years old at onset, the youngest on record. Another writer has observed a patient aged 64 who had his first attack at the age of 59.

The attacks of pain are intolerable. Fortunately their duration is relatively short, minutes to an hour; although an attack may continue for several hours. The constant boring or throbbing pain is located lateral to an eye a few centimeters behind and above the outer canthus. It may spread to involve the remainder of the cheek, the forehead, the temporal scalp, and rarely the neck. The pain usually affects the same side repeatedly, in fact the same spot. In contrast to the more usual migraine where the patient prefers to recline and pull the covers over his head, with Harris's migraine he cannot recline and usually must pace. There seems to be a relationship between the pain and the muscular activity that it occasions. There is congestion of the conjunctiva on the same side as the pain and sometimes stuffiness of the ipsilateral nostril. Flushing of the ipsilateral forehead and cheek have been seen occasionally. Vomiting practically never occurs. Some patients believe they may precipitate attacks in the same manner as do persons with trigeminal neuralgia, by chewing, washing their face, or brushing their teeth. Between attacks these people are well.

The attacks tend to occur at the same time of day or night. Characteristic is the pain that arouses a majority of these patients between 2 and 3 a. m. A bout usually lasts for weeks, during which the patient has at least one attack daily. He may have them every two hours or so, or the attack may become a "status migrainous," when he is rarely free of pain.

The bouts recur irregularly and then may cease after occurring for years. Ten of Bickerstaff's 30 patients had had attacks for over 10 years, two had them for 30 years.

Most of these patients have previously had a more classic form of migraine, which is replaced by the Harris form. In Bickerstaff's 11-year-old child the attacks of pain ceased spontaneously after two

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years and were replaced by ordinary migraine at the age of 16. Many patients give a history of migraine in near relatives.

Sir Charles Symonds[6] has devised a successful symptomatic treatment for Harris's migraine with regular prophylactic injections of ergotamine tartrate. The patient is taught to give himself intramuscular injections of ergotamine tartrate, 0.25 mg. three times a day, for five days in each week. The two free days allow the patient to determine whether the bout of pain has ceased. An occasional patient will require 0.5 mg. with each injection to obtain relief. While some patients vomit after early injections, this will cease after a few days without alteration of dosage. With this drug some patients are relieved of the Harris type of migraine but attacks of ordinary migraine then return. Ergotamine tartrate injections should be discontinued gradually rather than abruptly. Occasionally sudden withdrawal of the drug is accompanied by generalized headache. The usual precautions pertain about using these amounts of a potent vasoconstrictor substance.

There has been general agreement among neurologists that this type of head pain is a variant of migraine. The involvement is primarily if not exclusively of branches of the external carotid artery which dilate in a precipitate fashion. These patients cannot tolerate alcoholic drinks during periods when headaches are recurring, presumably because of their vasodilatory effect. Both Harold Wolff and Kunkle and their co-workers have been searching for the substance(s) released at the site of the pain in some forms of migraine. Some patients believe that, whatever it is, it may be "drawn off" or "drained away" by muscular activity.

Patients having Harris's migraine seem to have personality patterns comparable to those in patients with other types of migraine. Since there seems to be a great preponderance of patients having right-sided attacks, the problem might in some way be associated with handedness and eyedness. Right and left sidedness and its relation to personality is a fascinating study, as shown in Blau's[7] excellent monograph, "The Master Hand."

ORGANIZATION SECTION

ANNUAL CONFERENCE OF MENTAL HEALTH REPRESENTATIVES

On Nov. 20-21, 1959, the Council on Mental Health will hold its Sixth Annual Conference of Mental Health Representatives of State Medical Associations at the Drake Hotel in Chicago. The general theme of the conference, "Organized Medicine in Its Relationship to the Hospitalized Psychiatric Patient," will be divided into six group discussion areas: (1) in the state hospitals and other public mental hospitals area, (2) in the private mental hospitals area, (3) in the general hospitals area (psychiatric services in general hospitals), (4) in the outpatient psychiatric clinics area, (5) general rehabilitation services area, and (6) area of medicolegal aspects of commitment, discharge, and other court procedures relating to the mentally ill.

For the first time the Council will invite the commissioners of mental health of the 50 states to attend this year's conference. The Council feels the participation of the commissioners, along with the chairmen of the state association mental health committees, will make conference discussions and decisions, with respect to improvements that can be made in the care and treatment of the mental patient, much more effective.

The Council also intends to encourage subsequent meetings on this general theme at state levels to be organized and led by the state chairmen and commissioners jointly after the November conference.

Dr. John D. Porterfield, deputy surgeon general, U. S. Public Health Service, will be the guest speaker at the dinner meeting, Friday, Nov. 20.

BEQUEST TO RESEARCH FOUNDATION

The American Medical Research Foundation has received $12,274.71 from the estate of Miss Katherine Zimmerman of Monroe, Mich. C. Joseph Stetler, head of the A. M. A.'s law division, said the foundation may receive about $3,000 more if money held for taxes is not used by the estate. Miss Zimmerman, who died June 19, 1958, left 20% of the residue of her estate to the A. M. R. F.

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THE PRESIDENT'S PAGE

A MONTHLY MESSAGE

Most American physicians probably never have attended a state or national medical meeting at which there were no scientific exhibits, no scientific program, and no commercial displays. Recently I attended such a session, the second congress of the Brazil Medical Association held in the bustling city of over 600,000.

Despite the lack of scientific activities, approximately 500 Brazilian physicians, or 5% of the 10,000 membership, attended the meeting of the seven-year-old Brazilian Medical Association. For days—and nights—these physicians worked on socioeconomic problems in workshop conferences and in the House of Delegates.

I was invited to speak to the Brazilian physicians on the subject of the private practice system of medicine, free enterprise, voluntary health insurance, and the scope of government medicine in the United States. I was given an entire morning on the program. After my hour-long address, in which I explained, defended, and promoted our American system, I was asked scores of questions.

On the previous day the deputy minister of health of Great Britain was allotted the morning session to outline the British national health plan and to answer questions.

The two of us were the featured foreign speakers, and I assure you that we tangled verbally but amicably many times over the merits of our respective systems.

I believe that the young Brazil Medical Association and its member-physicians have great potential. With the freedom to function as an association of private practitioners and with the freedom to practice personal medicine as individual physicians, the association and doctors can bring the best medicine to the most people in Brazil. Of course, their challenges and opportunities are many, but having witnessed the physicians' dedication to work, I see no reason why the quantity and quality of medical progress there cannot be rapid and all-encompassing.

Already many Brazil hospitals are excellently equipped. The surgery I saw performed was as good as any I have seen in the United States. And Brazil has hundreds of well-trained physicians in all the specialties and in general practice.

As I saw it, however, Brazil's public health and sanitation facilities must be improved if many of the communicable diseases are to be prevented. For example, it is necessary to drink bottled water in all cities. Tropical diseases, too, are widespread and they are not being brought under control as rapidly as they probably could be.

The nation also has a medical school problem. While there are fine institutions in the country, there are many, many diploma mills in operation. These have arisen because there is no licensure of physicians.

Physicians of Brazil have expressed to me their desire of closer association with American medicine, and I hope that we can cooperate with them in solving some of the same health and medical education problems that we have had to deal with. They also would like to send more of their people here for training. This too I hope can be done in the interests of improved medicine and medical care in Brazil and in our Western Hemisphere. My experience in Brazil has warned me that if we do not offer our assistance, others certainly will.

Louis M. Orr, M.D.
Orlando, Fla.

COUNCIL ON NATIONAL DEFENSE

REGIONAL CD CONFERENCE

The central theme of the fifth regional meeting of the A. M. A. Committee on Disaster Medical Care was the heightened interest evident in preparedness for disaster when natural or industrial disaster, rather than the enemy inflicted nuclear holocaust, is emphasized. The Committee met in San Francisco on Sept. 26, 1959, with representatives of the medical societies of California, Nevada, and Utah of OCDM Region 7 and of Idaho, Oregon, and Washington which are in OCDM Region 8.

As at the four prior regional meetings of the Committee, the state reports on the status of medical preparedness for disaster ranged widely from that of California where planning, programming, and funding have resulted in a high degree of capability to Oregon with its funding and other problems and Idaho where the general lack of interest was recently dispelled somewhat by the Yellowstone National Park earthquake. It was agreed that the local disaster is the best stimulant to interest in medical as well as general public preparedness for disaster. A fire in Nevada in 1957 and a recent explosion in Oregon greatly stimulated disaster medical care activity as did the earthquake in Idaho. California has long emphasized preparation for natural disaster.

Prior regional meetings of the Committee on Disaster Medical Care of the Council on National Defense were held in Atlanta, Dallas, Boston, and Colorado Springs. The next meeting will be held in Chicago on Jan. 23, 1960.

COUNTY MEDICAL SOCIETIES CIVIL DEFENSE CONFERENCE

Medical and health personnel will be acquainted with some of the vital activities that local physicians and individual groups are doing in the field of medical preparedness for disaster at the conference at the Morrison Hotel in Chicago on Nov. 7-8, 1959.

Two reports at the conference will evaluate the hospital and medical disaster programs in operation during the school fire at Our Lady of the Angels' school in Chicago on Dec. 1, 1958, and the tornado which hit St. Louis this year. Top medical authorities will also report on preparedness and participation in civil defense programs in the federal government and at the state and local level. In addition, on Saturday afternoon, at workshop sessions, the conferees will discuss specific civil defense medical and health topics.

Highlights of the program will be talks by Congressman Melvin Price on the environmental and biological effects of nuclear attack, and by Major General Marshall Stubbs, chief chemical officer of the Army, on what everyone should know about chemical and biological warfare.

The registration fee of $10 includes two luncheons. Those planning to attend the conference are urged to register in advance by notifying the Council on National Defense, which annually sponsors this conference.

SAN ANTONIO'S MISSILE AGE HOSPITAL

The Office of Civil and Defense Mobilization has agreed to provide $300,000 for a nuclear survival complex to be built under the proposed $20,000,000 Southwest Texas Methodist Hospital at San Antonio. As reported in the April 1959 issue of the *Review*, the hospital will have in addition to its five stories above ground two floors below ground which will be constructed of reinforced concrete and will be designed to withstand any disaster. The hospital also will have its own power plant, underground water wells, and food stocks. In an emergency, the upper floors could be vacated and the hospital could operate for 30 days without access to the outside world. Other advanced features include a helioport where emergency patients can be flown by helicopter service; a closed-circuit TV system which will keep the nurse in contact with each patient; tele-thermometers capable of taking the patient's temperature from a distance; an electron beam generator which will disinfect virtually everything touched by human hands; and radar ranges to cook a full course meal by microwaves in 45 seconds.

REGIONAL CD UNDERGROUND CENTER

The First Session of the 86th Congress provided $2,400,000 to finance construction of a regional civil defense underground center at Denton, Texas. In the event of enemy attack, the center will insure decentralized federal guidance for Office of Civil and Defense Mobilization Region 5 which includes Texas, New Mexico, Oklahoma, Arkansas, and Louisiana. The facilities will also serve as an alternate National Control Center for civil defense should the OCDM establishments at Washington, D. C., and Battle Creek, Mich., be destroyed. The center will have a high degree of protection against blast and will be completely self-contained and permit sustained operations under adverse conditions of radioactive fall-out as well as chemical or biological warfare agents. The structure is planned to serve as a prototype for other regional defense headquarters.

DEPARTMENT OF ECONOMIC RESEARCH

SOME OBSERVATIONS ON FINANCIAL ASSETS OF THE AGED AND FORAND-TYPE LEGISLATION

Arthur Kemp, Ph.D., Leonard W. Martin, Ph.D.
and
Cynthia Harkness, B.A., Chicago

The famous British economist, Alfred Marshall, wrote many years ago: "Experience in controversies . . . brings out the impossibility of learning anything from facts till they are examined and interpreted by reason; and teaches that the most reckless and treacherous of all theorists is he who professes to let facts and figures speak for themselves. . . ."[1] The wisdom of this observation is forcefully brought home by an examination of the literature surrounding the report of the Department of Health, Education, and Welfare to the Committee on Ways and Means concerning hospitalization payments for beneficiaries of old age, survivors, and disability insurance (OASDI) and by the hearings conducted in July, 1959, by that committee on H. R. 4700 introduced by Rep. Aime J. Forand (D.) of Rhode Island. A striking feature of both the report and the testimony favoring the bill is the bias resulting from an almost complete lack of consideration of the assets of persons aged 65 and over and the almost exclusive emphasis on their cash income position.

Income—One of Many Measures

Even a cursory consideration of the problem should convince the reader that emphasis on money income tends to obscure the fact that many people aged 65 are at last reaching the time when they can retire on their savings. Why should it be difficult to understand that persons over 65 years of age, who have retired, have a lower income than those under 65 years of age who are still working and have not retired? Indeed, in a fairly prosperous society not devastated by inflation, one would expect a large proportion of those over 65 years of age and retired to be more comfortably off than those still at work.

Repeated again and again is the statement that about three-fifths of all persons 65 years or older had less than $1,000 money income in 1958. This statistic is presented in an article on money income distribution of the aged prepared by Lenore A. Epstein of the division of program research, Office of the Commissioner, Social Security Administration, which appeared in the June, 1959, issue of the *Social Security Bulletin.* Precisely the same statement was made by Wilbur J. Cohen before the Senate subcommittee on problems of the aged on June 16, 1959, and by Katherine Ellickson, assistant director of the Social Security Department of the AFL-CIO, as author of a bulletin issued June 23, 1959. On the same day Dr. Basil C. MacLean, president of the Blue Cross Association, stated in virtually the same words the same statistic at the University of Michigan's 12th Annual Conference on the Aging at Ann Arbor, Mich. Whether or not the source of these statements was the report of the Secretary of Health, Education, and Welfare to the Committee on Ways and Means one cannot say, but the statement does appear in the report dated April 3, 1959, on page 8: "Thus, both in 1956 and 1957 three-fifths of all people 65 and over had less than $1,000 in money income. . . ."[2]

Let us accept this statistic as a fact. Indeed, those who repeat it appear to accept it without question and to consider that it speaks for itself. This statistic, combined with the assumption that income is a sufficient measure of financial status, implies that the aged as a group suffer from poverty and privation because of their low incomes in a generally prosperous society. The implication can be questioned if one points out an equally accurate statistic, namely, that in 1957 almost one-half of all persons over 14 years of age also had incomes of $1,000 or less per year. Looking further one finds that 47% of all persons between the ages of 14 and 65 had incomes of $1,000 or less per year in 1957.[3] Yet, it also is true that the median family income in 1957 was approximately $5,000 per year.

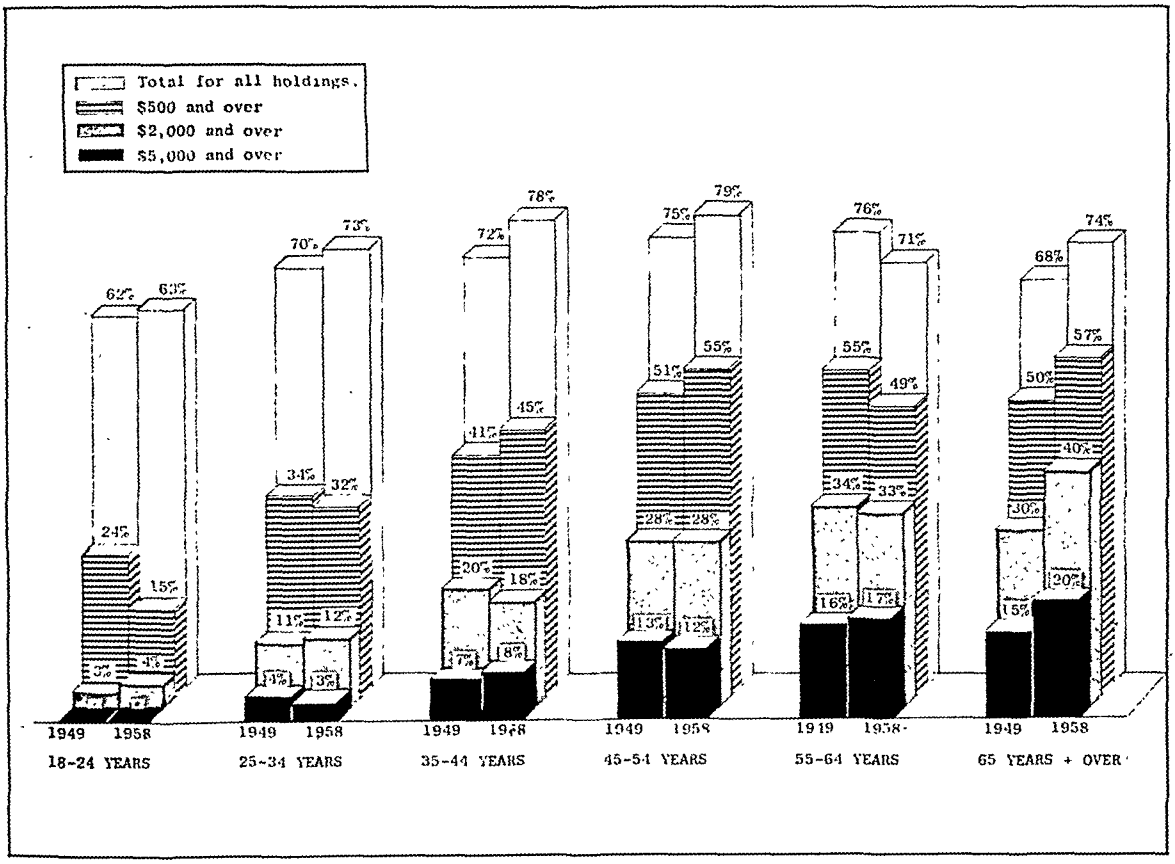
Misleading Arrangement of Data

Can all these things be true? Can there be a median family income of $5,000 per family while almost one-half of all persons earn $1,000 or less per year? The answer is yes. Both statements are true, and after a very little reflection it is not surprising that one can obtain such a high percentage of those aged 65 or over who have incomes of $1,000 a year or less, or even that one can obtain such a high percentage of all persons over the age of 14 years with such incomes. Parenthetically, of course, one would not be surprised to find the incomes of those under 14 years of age exceptionally low indeed, and for much the same reason.

Director (Dr. Kemp), Assistant Director (Dr. Martin), and Research Assistant (Miss Harkness), Economic Research Department, American

The important fact to be remembered is that the money income figures cited by the Department of Health, Education, and Welfare and others refer to individual and not to family income. In other words, let us imagine that a club is composed of a number of persons and their respective husbands or wives and that the conditions of membership in the club are (1) that only one member of each family be an income earner and (2) that the average income per family be in excess of $20,000 per year. This is the club. By using the same statistical technique or formulation as that employed by the Department of Health, Education, and Welfare, one-half (50%) of the members of that club have incomes of less than $1,000 per year (zero incomes, in fact) and, so long as the same conditions exist, will continue to have zero incomes even though the average income per person for the club has to be, by the very conditions of membership, in excess of $10,000 a year.

All of this leads to the conclusion that money income of the aged population, arranged on a per capita basis, is an insufficient and misleading measure of financial status. An appropriate measure of the aged's financial status should include also nonmonetary income, assets, and other resources.



Percentage distribution of liquid asset holdings of spending units, by age of head of spending unit, 1949 and 1958. (Source: *Fed. Res. Bull.* 35:911 [Aug.] 1949; 44:1055 [Sept.] 1958.)

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*No cases reported or less than ½ of 1%.

Growth in Assets of the Aged

An examination of the Federal Reserve Board's annual sample Survey of Consumer Finances reveals some interesting and supporting evidence concerning the aged's liquid assets and the rate at which those assets have been accumulating between 1949 and 1958. These are shown graphically in the figure. Between these two years, persons aged 65 and over accumulated liquid assets faster than any other age group. During this period the proportion of the aged group's ownership of liquid assets rose from 68 to 74%.[4] This means that in 1958 nearly three out of every four persons aged 65 or over owned liquid assets in some form. In contrast the percentage of persons 55 to 64 years of age who owned liquid assets dropped to 71% in 1958, while the average for all groups between the ages of 18 and 64 years rose from 71 to 73%.

The proportion of those aged over 65 who had liquid assets of $2,000 or more increased from 30% in 1949 to 40% in 1958; for liquid assets of $500 or more, the respective increase was from 50 to 57%. It should be noted that, generally speaking, the proportion of those over 65 years of age who have liquid assets of $500 or more, $2,000 or more, and

$5,000 or more is higher than for any other age group. The Federal Reserve Board's annual sample Survey of Consumer Finances also revealed that in 1958 the group aged 65 and over gained the highest median value in liquid asset holdings—$800 for all aged persons and $2,450 for the 74% holding liquid assets.[4a]

TABLE 1.—*Distribution of Liquid Asset Holdings and Incomes in Age Groups**

Age of Head of Spending Unit	Early 1958 Spending Units with Liquid Assets of More Than $500, %	Early 1958 Spending Units with Incomes of $3,000 or More, %
18 to 24	15	46
25 to 34	33	81
35 to 44	45	85
45 to 54	54	80
55 to 64	50	58
65 or over	56	27

* Source: The Financial Position of Consumers, Federal Reserve Bulletin 44:1052 (Sept.) 1958, and correspondence with James N. Morgan, Ph.D., Program Director, University of Michigan Survey Research Center, Ann Arbor, Mich.

It should be emphasized that these are the gross data for liquid assets only. Liquid assets, as defined by the Consumer Finances Survey, include savings accounts in banks, postal savings accounts, shares in savings and loan associations and credit unions, checking accounts, and savings bonds. Excluded are homes and other real estate, stocks, and bonds other than savings bonds. If it were possible to take into account ownership of equity securities and less liquid assets, the discrepancy in asset holdings between the aged and others probably would be even greater than the liquid asset data alone can illustrate. This observation follows from the fact that generally the aged have more of such assets than is commonly realized. Moreover, their net asset position is clearly better than that of others since their indebtedness is low and their homes are characteristically owned mortgage-free.

The aged are above average in the percentage of persons having savings in liquid form, and this percentage has been shifting in favor of the aged group although the younger age groups would normally be thought to have a greater earning power. In September, 1958, the *Federal Reserve Bulletin* concluded that "There was a marked tendency . . . for the frequency of large holdings—particularly of savings accounts or shares—to increase with age. One-half of the savings deposit holders who were 65 or older had $2,400 or more in this form, compared with a median of $720 for all holders."[5]

The Relation of Assets, Income, and Age

One normally expects to find a positive correlation between annual money income and the size of liquid asset holdings. But, here again, because the logical relationship is between liquid asset holdings and total money income earned over a lifetime rather than annually, the correlation cannot be expected to be as high for those in the age group over 65, a large proportion of whom have retired. Surely there is a relationship between savings and income; but more significant is the relationship of age to savings despite the relationship of age to income.

Table 1 provides distributions of both liquid asset holdings and incomes with respect to age and reveals most clearly that savings tend to rise almost continuously with age. The percentage of spending units with liquid assets of more than $500 early in 1958 rose with age except for the age group 55 to 64, which is reported to be an age group severely hit by the 1957-1958 recession.

The relationship of income to age is considerably different from that of savings to age. Consequently, asset holdings did not move in the same direction as income for all age groups. The percentage of spending units with an income of $3,000 or more rose over the three youngest age groups, fell slightly for the fourth, and declined sharply for the groups aged 55 and over. Yet the percentage with liquid assets of $500 or more continued to rise through age 54 and slipped only slightly for the age group 55 to 64, despite the sharp decline in percentage of units with incomes over $3,000 for that group. Moreover, the percentage of those with incomes of $3,000 fell sharply in the 65 and over age group, while savings (liquid asset holdings of $500 or more) reached the highest percentage in this age group.

When, as in table 2, the asset holding data are arranged within income groups, some further evidence of the relationship of income to savings is revealed. In every respect the percentage of spending units with any assets at all or of the specified sizes was greater when the income was greater—$3,000 to $5,000 as compared with those of $3,000 or less. However, with rare exceptions the percentages of spending units with assets increased with the age of the head of the spending unit. The

TABLE 2.—*Relation Between Age, Income, and Savings**

Age of Head of Spending Unit	% Who Are Liquid Asset Holders	% with Liquid Assets of $500 or More	% with Liquid Assets of $2,000 or More
Spending Units with Incomes of $3,000 or Less, 1958			
18 to 24	51	5	†
25 to 34	34	16	3
35 to 44	45	23	5
45 to 54	46	26	12
55 to 64	51	26	16
65 or over	65	45	30
Spending Units with Incomes Between $3,000 and $5,000, 1958			
18 to 24	72	17	6
25 to 34	67	21	6
35 to 44	68	27	10
45 to 54	78	49	24
55 to 64	72	46	31
65 or over	90	81	57

* Source: Derived from table LAT 9, Study 666, for the Economic Behavior Program, University of Michigan Survey Research Center, Ann Arbor, Mich., 1958, unpublished data.

† Less than 0.5%.

exceptions occurred only in the 18 to 24 and 55 to 64 age groups. Evidently savings are not determined by income alone.

Indeed the size of the percentages for the group aged 65 and over is striking. While almost 75% of the aged had incomes of $3,000 or less (in 1957), nearly half of them in this income bracket owned liquid assets of $500 or more in 1958, and 30% had liquid assets valued over $2,000. Similarly the aged had the highest percentages among those with incomes ranging between $3,000 and $5,000. Eight of every 10 spending units in the age group 65 and over held assets of $500 or more and 57% had liquid holdings valued at $2,000 and above.

This does not mean, of course, that all persons over 65 years of age are rich and all those under 65 poor. It does suggest, however, that the problem of the aged is not simply one of age, or even one of money income and age. The problem is not a group problem; to the extent that it can be argued that some persons cannot afford medical care, the argument calls for either an extension of the deductible provision in income tax laws or, at most, for some subsidization of the poverty-stricken.

Conclusions

It should be apparent that the use of money income alone in assessing the financial status of those over 65 years of age may lead to erroneous conclusions. The relatively substantial liquid assets of those over 65 years of age are of great importance. These observations raise some questions as to the desirability, and even the sincerity, of legislative proposals designed to compel those under 65 years of age to pay for the medical care costs of those over 65, regardless of financial status. Certainly, in many individual cases those over 65 are better able to afford medical care than those under that age.

Physicians and others whose efforts are devoted to providing the best quality of medical care and to preserving and extending human life should not overlook the implications of programs drawn up by an alliance of "experts" with a vested interest in governmental activities and politicians seeking election or reelection. There are indeed chronic problems of aging and the aged, but, above all else, they are individual problems of individual human beings. Moreover, if governments will refrain from engaging in activities sure to destroy the purchasing power of people's accumulated dollars, the problem, at most, is temporary. Instituting a permanent program and a new bureaucracy to provide governmental health care for the aged, regardless of need, supplies a "cure" that may be worse than the "disease" in its ultimate effects on individual freedom and a free society.

Alfred Marshall, whose astute words were quoted above, raised the pertinent question more than a quarter century ago when he asked:

> Why should it be left for impetuous socialists and ignorant orators to cry aloud that none ought to be shut out by the want of material means from the opportunity of leading a life that is worthy of man? Of those who throw their whole souls into the discussion of this problem, the greater part put forth hastily conceived plans which would often increase the evils that they desire to remedy. . . .[6]

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GOVERNMENT SERVICES

NAVY

Navy Flight Surgeons.—If you have not been receiving your copy of *'Contact,'* the annual news magazine published by the Naval School of Aviation Medicine, please send your name and address to the editor, Capt. Philip B. Phillips, M. C., U. S. N., Naval Aviation Medical Center, Pensacola, Fla., so you may be put on the mailing list. The latest issue was distributed in October.

PUBLIC HEALTH SERVICE

Symposium on Venereal Diseases.—The Eleventh Annual Symposium on Recent Advances in the Study of Venereal Diseases will be held April 7 and 8, 1960, in the Palmer House, Chicago. The sessions will be open to all physicians and workers in allied fields who are interested in the venereal diseases. This symposium, sponsored jointly by the American Venereal Disease Association and the Public Health Service, will follow a venereal disease seminar for public health personnel which begins April 4. Anyone wishing to present a scientific paper on a subject related to venereal diseases should mail preliminary abstracts before Nov. 25 to Dr. William J. Brown, program committee chairman, in care of the Venereal Disease Branch, Communicable Disease Center, 50 Seventh St., N. E., Atlanta 23, Ga. Preliminary abstracts should give information sufficient to assist the program committee in making a decision as to their acceptance or rejection. Authors of accepted papers will be notified before Jan. 15. Final abstracts not exceeding 500 words will be required by March 1.

MEDICAL NEWS

ALASKA

Increase in Poliomyelitis.—Between Jan. 1 and Sept. 1, a total of 12 cases of poliomyelitis in Alaska were reported to the Alaska Division of Health. Only two cases were reported for the entire year of 1958. Seven of the 1959 cases were in Eskimos from the lower Kuskokwim River Area. Nine of the patients were infants 15 months to 3 years of age, two were children 7 and 9 years old, and one was a 47-year-old man. More than half of the cases were reported as paralytic, whereas the type of poliomyelitis was not stated for four and one was described as nonparalytic. In August a member of a group of 60 student tourists died of bulbar poliomyelitis at Whitehorse, Canada, en route from Fairbanks. After a temporary shortage of vaccine, the Division of Health supply was replenished in August.

CALIFORNIA

Annual Scientific Symposium.—The San Diego Academy of General Practice will hold its annual scientific symposium at the Hotel Riviera, Las Vegas, Nev., Nov. 12-14. Speakers on the program are as follows: Dr. Charles W. Mayo, Rochester, Minn.; Dr. William P. Thompson, Los Angeles; Dr. James E. M. Thomson, Lincoln, Neb.; and Dr. Robert E. Ryan, St. Louis, Mo. The banquet is planned for Nov. 12, 8 p. m. The symposium is approved for category I credit by the American Academy of General Practice. For information, write Dr. Harold P. Peterson, 5950 El Cajon Blvd., San Diego 15, Calif.

COLORADO

Open University Hospital Service.—The new Wardenburg Student Health Center, offering the University of Colorado Boulder campus its first hospital service in 33 years, opened Sept. 21. The million-dollar sandstone infirmary has a staff of 52 including physicians, nurses, and technicians. A gift from alumni Mr. and Mrs. F. A. Wardenburg, Wilmington, Del., it fills a gap in medical care that the university has felt since the medical school moved to Denver in 1925. Students, who previously obtained hospital care from downtown Boulder facilities, with costs partly paid through student health insurance, will have access to the new campus hospital facilities without additional cost. Serious illness and surgery will be treated at off-campus hospitals. The new building offers almost full hospital and clinical care.

CONNECTICUT

Dr. Dublin Receives Health Medal.—Louis I. Dublin, Ph.D., Westport, is the 1959 recipient of the American Public Health Association's Sedgwick Memorial Medal "for distinguished service in public health." Dr. Dublin retired as second vice-president and statistician of the Metropolitan Life Insurance Company in 1952 after 43 years with the company, and since then has served as consultant to the Institute of Life Insurance on community health and welfare activities.

FLORIDA

Dr. Anderson Honored.—Dr. William A. D. Anderson, chairman, department of pathology, University of Miami School of Medicine, Coral Gables, received the annual award of the Scientific Products Foundation "for the most outstanding contribution to the improvement of laboratory techniques." The award was presented by the College of American Pathologists, of which Dr. Anderson is a past-president.

ILLINOIS

General Practice Meeting in Chicago.—The 12th annual scientific assembly of the Illinois Academy of General Practice will be held Nov. 9-12 at the Morrison Hotel, Chicago. The Congress of Delegates will meet Nov. 9 with Dr. Mladen Mijanovich, of Marengo, speaker, presiding. Dr. Robert E. Heerens, Rockford, president of the academy, will open the first scientific session with an address. Papers to be presented by out-of-state speakers include the following:

Heart Disease the World Over, Dr. Paul Dudley White, Boston.
Management of the Listless Patient, Dr. Paul E. Craig, Tulsa, Okla.
The Treatment of Insomnia by the General Practitioner, Dr. Leo H. Berman, Norwalk, Conn.
Common Sense Approach to Diagnosis of Fluid Imbalances, Dr. William D. Sniveley Jr., Evansville, Ind.
Mucolytic Agents in the Therapy of Respiratory Diseases, Dr. Meryl M. Fenton, Detroit.
Practical Considerations in the Prophylaxis of Rabies, Dr. Franklin B. Peck Jr., Indianapolis.
Carcinoma of the Thyroid; A Therapeutic Problem, Dr. John W. Cline, San Francisco.
Hormone Therapy in Early or Questionable Pregnancy, Dr. Harold A. Schwartz, Chattanooga, Tenn.
ACTH and Corticosteroids in Allergy, Dr. Stanley F. Hampton, St. Louis.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Two panel discussions are planned: "Hospitals—the Privileges and Responsibilities of the Medical Staff Which Especially Concern the G. P." and "Steroids—When Are They Useful? Are They Harmful?" The annual dinner dance will be held Nov. 11, 7:30 p. m. Exhibits are planned. The program is acceptable for 10 hours category I credit. For information, write the Illinois Academy of General Practice, 14 E. Jackson Blvd., Chicago 4.

Chicago

Hospital Anniversary Program.—The medical staff of Mount Sinai Hospital celebrated the 40th anniversary of the hospital founding with a scientific program Oct. 30 in the Leopold Kling auditorium of the nurses' residence. The speakers were Dr. Ben W. Lichtenstein, president of the medical staff and attending neuropsychiatrist; Homer W. Smith, Sc.D., professor of physiology, New York University–Bellevue Medical Center. Dr. Lichtenstein presented "Multiple Sclerosis" and Dr. Smith, "Sodium: Five Hundred Million Years of Struggle with Too Little or Too Much."

Symposium on Cerebral Vascular Disease.—The Chicago Heart Association will present a symposium on cerebral vascular disease at the Knickerbocker Hotel, Saturday, Nov. 7, 2-5 p. m. Dr. J. C. Paterson, professor of medical research, University of Western Ontario, London, Canada, will serve as chairman of the program, which includes the following papers and speakers:

Cerebral Atherosclerosis—Histopathology, Pathogenesis, and By-Products, Dr. Matthew T. Moore, Philadelphia.
The Clinical Pattern in Certain Types of Occlusive Cerebral Vascular Disease, Dr. Clark H. Millikan, Rochester, Minn.
Recent Trends in the Therapy of Cerebral Vascular Disease, Dr. Sigmund N. Groch, New York City.

The following Chicago physicians will serve as discussants on the program: Drs. Orville T. Bailey, Wendel J. S. Krieg, Irving C. Sherman, Richard B. Richter, and Raymond A. Clasen. For information, write the Chicago Heart Association, 22 W. Madison St., Chicago 2.

Meeting to Discuss Internship.—A nationwide meeting on "The Future of the Internship" will be convened at Michael Reese Hospital and Medical Center, Saturday, Nov. 28. The special session, to which medical students, physicians, and educators have been invited, will take place in Rothschild Auditorium, 2816 Ellis Ave., from 9:30 a. m. to 12:45 p. m. Dr. Rachmiel Levine, director of medical education at Michael Reese, stated that "The program is an attempt to evaluate which type of postgraduate training is best suited to present-day medicine." The internship of the present and two views of its future will be discussed by Dr. E. Hugh Luckey, chairman, department of medicine, Cornell University Medical College, New York City, and Dr. Victor Johnson, Rochester, Minn., director of the Mayo Foundation for Medical Education and Research. "The Internship as It Appears to Today's Interns" will be reviewed by Dr. Richard H. Saunders Jr., Rochester, N. Y., director of the internship study, Association of American Medical Colleges. A panel discussion will complete the half-day session. The meeting is open to interested medical and educational personnel. It is sponsored by the administration of Michael Reese.

KANSAS

Dr. Frederickson Appointed Section Head.—The University of Kansas School of Medicine in Kansas City announced the appointment of Dr. Evan L. Frederickson to the staff as head of the section of anesthesiology and professor of surgery, effective Sept. 1. He was an assistant professor in anesthesiology in that section from 1953 to 1955. Dr. Frederickson comes to Kansas from the University of Washington, Seattle, where he was associate professor in pharmacology and anesthesiology.

MASSACHUSETTS

Dedicate Industrial Rehabilitation Unit.—The newly completed Industrial Rehabilitation Unit of the Boston University–Massachusetts Memorial Hospitals Medical Center, located on the seventh floor of Robinson Building at 750 Harrison Ave., was dedicated Oct. 1. The unit is headed by Dr. Henry J. Bakst, of Brookline, chief of the rehabilitation unit. It serves as a training facility for physicians, nurses, social workers, physical therapists, and medical students and provides care for patients with severe handicaps. The unit was formerly housed at Haynes Memorial Hospital.

MICHIGAN

Annual General Practice Meeting.—The 13th annual fall Postgraduate Clinic presented by the Michigan Academy of General Practice and the Wayne County Academy of General Practice will be held Nov. 11-12 at the Sheraton-Cadillac Hotel, Detroit. Dr. Clark W. Royer, Battle Creek, president of the Michigan academy, will preside at the first session. The program is arranged as a series of symposiums and panel discussions under the following titles:

Symposiums
  Modern Therapy
  Cardiovascular Disease
  Obstetrics
  Tranquilizers
  General Medicine
Panels
  Burn Therapy
  Corticosteroids in General Practice
  Newer Therapy

Scientific and technical exhibits are planned. The program includes 33 guest speakers. There is no registration fee, and academy members will be allowed 11 hours category I credit for attendance. For information, write Dr. Francis P. Rhoades, 970 Maccabees Building, Detroit 2.

MINNESOTA

Lecture by New Zealand Surgeon.—Mr. Douglas Robb, senior thoracic surgeon to the Green Lane Hospital in Auckland, New Zealand, and prochancellor of the University of Auckland, delivered the 12th annual Judd-Plummer Memorial Lecture at the 37th annual meeting of the Alumni Association of the Mayo Foundation in Rochester. Mr. Robb presented "The New Zealand Medical Service: An Appraisal" on Oct. 9.

Name Executive Director for Medical Foundation.—Mr. Eivind Hoff Jr., Minneapolis, was named executive director of the Minnesota Medical Foundation, a nonprofit faculty-alumni-public group serving the Medical School at the University of Minnesota. The 1,200-member foundation, established in 1930, annually awards about two dozen scholarships to university medical students; raises funds for various programs supporting the school; and publishes a biweekly scientific journal, *the University of Minnesota Medical Bulletin*. Mr. Hoff, first full-time staff person in two decades of foundation history, was director of professional education and public relations for the Minnesota Heart Association since 1955.

NEVADA

State Medical Election.—The following is the result of election of officers of the Nevada State Medical Association at the annual meeting in Reno Aug. 22: Dr. Ernest W. Mack, Reno, president; Dr. Wesley W. Hall, Reno, president-elect; Dr. William A. O'Brien III, Reno, secretary-treasurer; Dr. Earl N. Hillstrom, Reno, alternate delegate to the A. M. A.; and Dr. Roland W. Stahr, Reno, immediate past-president. Dr. Hall will also serve as delegate to the A. M. A. House of Delegates.

NEW YORK

Graduate School of Psychiatry.—The New York State Department of Mental Hygiene opened a graduate school of psychiatry devoted to basic and advanced psychiatric education for its medical personnel on Sept. 14. Known as the New York School of Psychiatry, the school operates under a provisional charter granted by the board of regents of the University of the State of New York and offers a three-year training program. Prior to the completion of the organization of the school, the program was operated temporarily on a two-year basis. The new school serves the staffs of Brooklyn, Creedmoor, Kings Park, Pilgrim, and Central Islip state hospitals and Willowbrook State School. The graduate school is quartered in the medical-surgical building of Manhattan State Hospital on Ward's Island, where its teaching facilities include an outpatient clinic. Instruction includes a basic curriculum in psychiatry and advanced curriculums in specialized areas.

New York City

Dr. Meyer Honored.—The annual T. Duckett Jones Memorial Award, in the amount of $6,500, was presented to Dr. Karl Meyer, Columbia University College of Physicians and Surgeons, at the annual meeting of the Helen Hay Whitney Foundation research fellows and established investigators Sept. 26. This award was presented "in recognition of Dr. Meyer's pioneer and continuing work in the field of mucopolysaccharides." Dr. Meyer's work has included the first isolation of hyaluronic acid. Acquisition of new knowledge in the disease of connective tissues is the objective of the Helen Hay Whitney Foundation's program of support for "research fellows and established investigators of promise who desire an academic career as clinical investigators or scientists in the study of connective tissues and their diseases."

Personal.—Dr. Morris Schaeffer was named director of the Bureau of Laboratories of the City of New York Department of Health. Dr. Schaeffer comes from the Communicable Disease Center of the U. S. Public Health Service, Montgomery, Ala., where he served as medical director in charge of the Virus and Rickettsia Section.——Drs. John J. Kelly Jr. and J. Leonard Brandt resigned Aug. 31 as associate professors of medicine at the State University of New York Downstate Medical Center in Brooklyn. Dr. Kelly will become director of medical education at Mercy Hospital in San Diego, Calif., while Dr. Brandt has been named physician in chief of the Jewish General Hospital and director of medical research and lecturer in medicine at Magill University, Montreal.——Dr. J. Hamilton Crawford, clinical professor of medicine at the State University of New York Downstate Medical Center in Brooklyn, retired from active service on the faculty in August and was named clinical professor emeritus of medicine effective Sept. 1. Dr. Crawford has been a member of the faculty for over 30 years.——Dr. Charles L. Ravaris, Detroit, was appointed an assistant medical director of E. R. Squibb & Sons, Dr. Lawrence B. Hobson, medical director, announced.

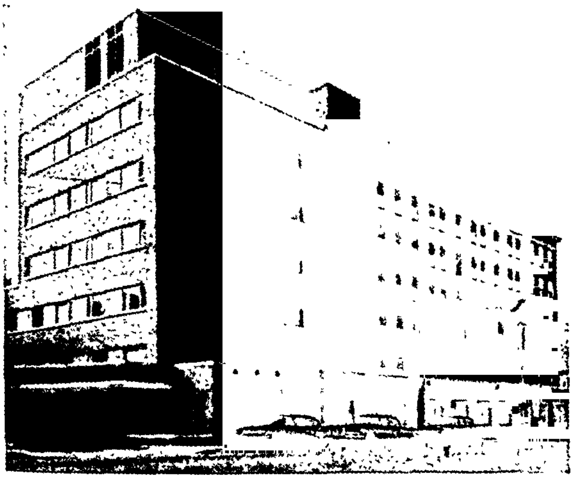
NORTH CAROLINA

Campaign to Build Research Center.—Alumni of the Bowman Gray School of Medicine of Wake Forest College have set $500,000 as their goal in a campaign to build a new Research Center in Winston-Salem. Dr. George W. Paschal Jr., of Raleigh, is general chairman of the Research Center Fund.

The proposed five-story Research Center Building will be a wing added to the recently built James A. Gray Memorial Building, which doubled the school's space when it was opened in 1958.

NORTH DAKOTA

Dedicate Hospital Addition in Minot.—Dedication ceremonies for the six-story, $2,500,000 addition to Trinity Hospital, Minot, were held Sept. 27, with Dr. Russell A. Nelson, Baltimore, president of the American Hospital Association and director of the Johns Hopkins Hospital, as the principal guest speaker. The institution now has a bed capacity of 250, reportedly making it the largest voluntary hospital in North Dakota. On the first floor of the addition and the remodeled original building are housed radiology, pathology, and bacteriology laboratories, a pharmacy, an emergency unit adjacent to the ambulance entrance, a central supply depot, and the surgical suite. The latter provides eight major operating rooms, including two designed and equipped for urological and orthopedic surgery. The postoperative recovery rooms provide care for eight patients at a time. On the second floor are the rehabilitation wing, with 43 beds, and the division of physical medicine, including the departments of physical therapy, hydrotherapy and electrotherapy. Funds for the addition and remodeling were provided by private donors and the Hill-Burton Act in the amount of $325,000.



The new six-story addition to Trinity Hospital, Minot.

PENNSYLVANIA

Annual Lecture.—The Phi Delta Epsilon Fraternity, Nu Chapter, plans to hold the 14th annual R. R. Huggins Memorial Lecture on Nov. 5 at Nu Chapter, Pittsburgh. The speaker will be Dr. William Dameshek, Blood Research Laboratory, New England Center Hospital, Boston. The subject will be "Polycythemia Vera and Related States."

Tuberculosis Director Retires.—Dr. Morrison Clay Stayer, Harrisburg, director of the State Health Department's tuberculosis control program for 13 years announced his retirement, effective Sept. 4. Dr. Stayer was appointed to the State Health Department in August, 1946, following his retirement from a 38-year career in the United States Army Medical Corps. Dr. Harold E. Coder, Harrisburg, succeeds Dr. Stayer as director of the State Division of Tuberculosis Control. He has been chief of the tuberculosis hospitals under the administration of the State Department of Health.

Philadelphia

Annual Conference for Ex-Residents.—The 12th annual clinical conference of the staff and Society of Ex-Residents of Willis Eye Hospital will be held on Feb. 18-20, 1960. Clinic and hospital rounds will be held the morning of Feb. 18 and special surgical clinics in the afternoon. On the evening of Feb. 18, there will be a scientific meeting of the ophthalmological section of the Philadelphia College of Physicians which will be preceded by dinner. Dr. Levon K. Garron, of Oakland, Calif., will be the guest speaker. On Feb. 19 the scientific program will include individual presentations and color television surgery. The Arthur J. Bedell Lecture will be delivered on Feb. 20 by Dr. Peter C. Kronfeld, of Chicago. The conference will be concluded by a dinner meeting of the society that evening.

GENERAL

Clinical and Climatological Meeting.—The 72nd meeting of the American Clinical and Climatological Association will be held Nov. 2-4 at the Homestead, Hot Springs, Va. Dr. George W. Thorn, Boston, will present the presidential address preceding the presentation of formal papers. The Gordon Wilson Lecture, "Studies on the Effect of Vitamin B_1 Deficiency on the Human Nervous System," will be given by Dr. Raymond D. Adams, Boston. Seventeen other papers are scheduled. A business meeting is planned for the morning of Nov. 4. For information, write Dr. Fred T. Billings Jr., 420 Medical Arts Building, Nashville 12, Tenn.

Meeting on Fractures in New Orleans.—The American Fracture Association will hold its 20th annual meeting Nov. 1-4 at the Roosevelt Hotel, New Orleans, with the program acceptable for category II credit by the American and Louisiana academies of general practice. Industrial courses Nov. 1 will be acceptable for category I. Dr. Duncan C. McKeever, Houston, Texas, president of the association, will open the meeting and moderate the first session. Fifteen round-table discussions are planned for the afternoon of Nov. 1. A symposium, "External Pinning," will be moderated by Dr. Alvin H. Diehr, St. Louis. A second symposium, the H. D. Junkin, M.D., Memorial, on the subject, "Ostamer," will be moderated by Dr. Earl D. McBride, Oklahoma City, Okla. For information, write Dr. Hermann W. Wellmerling, 610 Griesheim Bldg., Bloomington, Ill., Executive Secretary.

Meeting of Inhalation Therapists.—The fifth annual meeting and lecture series of the American Association of Inhalation Therapists will be held Nov. 16-20 at the Benjamin Franklin Hotel, Philadelphia. The five-day meeting will include medical lectures, round-table discussions, a field trip to a hospital, and the annual business meeting and election of new officers. The A.A.I.T. is a paramedical association whose objective is "to advance the art and science of inhalation therapy in the treatment of pulmonary and heart disorders." It is sponsored by the American College of Chest Physicians and the American Society of Anesthesiologists. It has 18 chapters and about 800 members in the United States and Canada. A featured speaker will be Dr. Kenneth L. Stratton, medical director, American Airlines, Inc., Flushing, N. Y., who will discuss "Oxygen and the Space Age."

Meeting on Gastroenterology Research.—The ninth semi-annual meeting of the Gastroenterology Research Group will be held Nov. 6 at the Drake Hotel, Chicago. A symposium, "The Biology of the Colonic Mucosa," will be moderated by Dr. Thomas P. Almy, New York City. Four papers are scheduled for presentation as follows:

Cellular Proliferation and Renewal in the Colonic Epithelium, Bernard Messier, Ph.D., Montreal, Canada.

Healing of the Colonic Mucosa, Dr. George D. Lumb, Memphis, Tenn.

The Role of the Normal Intestinal Flora in Antibody Production, Dr. Helmut A. Gordon, Niles, Mich.

Hypersensitivity Reactions in the Colonic Mucosa, Dr. Joseph B. Kirsner, Chicago.

A general session will follow the papers. The gastroenterology research dinner will be held at 5:30 p. m. The 10th semiannual meeting of the group will be held at the Roosevelt Hotel, New Orleans, March 31, 1960.

Southern Medical Meeting in Atlanta.—The Southern Medical Association will meet Nov. 16-19 at the Atlanta Municipal Auditorium, Atlanta, Ga., under the presidency of Dr. Milford O. Rouse, Dallas, Texas. Four major general sessions and 20 section meetings are scheduled. Two of the general sessions, one in medicine and one in surgery, will be presented Nov. 16. The others, in geriatrics and in nuclear medicine, will be presented Nov. 19. The Southern Flying Physicians and other socieites will meet conjointly. Scientific color television programs will be held Nov. 16-18. The annual dinner dance will be held Nov. 18, 7 p.m. Scientific and technical exhibits are planned, and a ladies' program is arranged. The annual golf tournament will be held Nov. 16-17. A postconvention tour to Nassau is planned. For information, write the Southern Medical Association, 2601 Highland Ave., Birmingham 5, Ala.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	Oct. 3, 1959		Oct. 4, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	4	4	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	8	9	3
Rhode Island	..	..	..
Connecticut	2	2	..
Middle Atlantic States			
New York	22	29	13
New Jersey	6	8	18
Pennsylvania	15	18	5
East North Central States			
Ohio	9	12	35
Indiana	5	13	7
Illinois	6	17	17
Michigan	13	30	98
Wisconsin	5	5	6
West North Central States			
Minnesota	15	20	2
Iowa	6	9	6
Missouri	11	16	8
North Dakota	..	1	3
South Dakota	..	..	..
Nebraska	3	6	1
Kansas	3	5	..
South Atlantic States			
Delaware	..	..	..
Maryland	3	3	1
District of Columbia	..	..	..
Virginia	6	8	3
West Virginia	6	6	11
North Carolina	12	19	9
South Carolina	2	5	1
Georgia	8	12	..
Florida	1	2	3
East South Central States			
Kentucky	19	21	4
Tennessee	29	34	5
Alabama	3	3	1
Mississippi	..	..	11
West South Central States			
Arkansas	7	10	1
Louisiana	4	7	1
Oklahoma	5	6	2
Texas	2	9	18
Mountain States			
Montana	..	..	3
Idaho	..	..	..
Wyoming	..	..	..
Colorado	1	1	2
New Mexico	1	1	..
Arizona	..	1	1
Utah	..	..	2
Nevada	..	1	..
Pacific States			
Washington	13	13	..
Oregon	8	10	..
California	16	17	12
Alaska	..	..	..
Hawaii	..	..	2
Territories and Possessions			
Puerto Rico	..	1	..
Total	279	394	315

Obstetricians and Gynecologists Meet in Hawaii.—The sixth annual meeting of District VIII, The American College of Obstetricians and Gynecologists, will be held at the Royal Hawaiian Hotel, Honolulu, Hawaii, Nov. 15-22. District VIII comprises Alaska, Arizona, California, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, Wyoming, Alberta, British Columbia, and Hawaii. The scientific program will consist of 15 formal papers, 20 round tables, and 45 breakfast conferences. Two days will be devoted to visits to hospitals and clinics in Honolulu. Dr. George E. Judd, Los Angeles, District VIII chairman, will open the meeting. Among the participants in the scientific program will be Drs. John I. Brewer, Chicago, president of ACOG; Robert G. Craig, San Francisco, immediate past-president; and Craig W. Muckle, Philadelphia, secretary. The entertainment program includes a luau and dinner dance. For information, write Dr. George E. Judd, 2010 Wilshire Blvd., Los Angeles 57, or Mr. Donald F. Richardson, executive secretary, ACOG, 79 W. Monroe St., Chicago 3.

Medical Imposter.—One Clarence H. Cypher has represented to the Board of Medical Examiners of the State of Arizona and to others that he is a doctor of medicine. Cypher is described as having obtained money from several persons on the representation that he is a physician. A thorough check of the biographic records at A. M. A. headquarters, however, does not reveal that a man by that name has ever been a medical student or a graduate in medicine. Cypher is described as one acquainted with medical terminology and customs, possibly acquired while employed as a technician or in some similar paramedical capacity. He is between 35 and 38 years of age, about 5 ft. 7 in. in height, weighing 135-140 lbs., thin, having a long, sharp nose, blue eyes, and gray hair. Cypher has represented himself as a physician in Douglas and Phoenix, Ariz., and Germantown, Ky. He has claimed graduation from the University of Michigan Medical School and/or the Chicago Medical School. Anyone having knowledge of his whereabouts should contact the Department of Investigation at A. M. A. headquarters or the Executive Secretary of the Board of Medical Examiners of the State of Arizona at Phoenix.

Annual Symposium on Antibiotics.—The seventh annual Symposium on Antibiotics, sponsored by the journals *Antibiotics & Chemotherapy* and *Antibiotic Medicine & Clinical Therapy*, will be held Nov. 4-6 at the Mayflower Hotel, Washington, D. C. The symposium will open with a general session dedicated to "The Challenge of New Drugs in Our Society." Dr. Felix Marti-Ibanez, New York City, will inaugurate this session with a talk, "The Great Historical Challenges in Medicine," and Drs. Austin E. Smith, Washington, D. C., Maxwell Finland, Boston, William H. Kessenich, Washington, D. C., and John G. Quarry, Burlington, Ont., will discuss the following: "The Challenge of New Drugs to the Pharmaceutical Industry," "The Challenge of New Drugs to the Clinical Investigator," "The Challenge of New Drugs to the U. S. Food and Drug Administration," and, finally, "The Challenge of New Drugs to the Practicing Physician." Two panel discussions are planned: The Present Status and Problems Involved in Human Sensitization to Antibiotics, and Chemotherapy of Acute and Chronic Pediatric and Geriatric Infections. For information, write Henry Welch, Ph.D., Director, Division of Antibiotics, Food and Drug Administration, U. S. Department of Health, Education, and Welfare, Washington 25, D. C.

Postgraduate Medical Meeting.—The 44th international medical assembly of the Interstate Postgraduate Medical Association of North America will be held Nov. 2-5 at the Palmer House, Chicago. The program includes the following panel discussions and moderators:

Massive Intestinal Hemorrhage, Dr. Alton Ochsner, New Orleans.
Renal Failure, Dr. Robert M. Kark, Chicago.
Emergencies in the First Day of Life, Dr. Willis J. Potts, Chicago.
Non-Toxic Goiter, Dr. George Crile Jr., Cleveland.
The Place of Pitocin in Obstetrical Practice, Dr. Herbert E. Schmitz, Chicago.
Resistant Staphylococcus Infections, Dr. Edgar J. Poth, Galveston.
Medical Aspects of Modern Submarine Warfare, Capt. Gerald J. Duffner, MC, USN, Washington, D. C.
Newer Developments in Diuretics, Dr. John H. Moyer, Philadelphia.
Treatment of Multiple Injuries Associated with Auto Accidents, Dr. George J. Curry, Flint, Mich.
Evaluation of the Acute Abdomen, Dr. Robert M. Zollinger, Columbus, Ohio.

A surgical symposium is planned for the afternoon of Nov. 4, at which Dr. Samuel F. Marshall, Boston, will present "Carcinoma of the Stomach" as the Arthur G. Sullivan Memorial Lecture. Breakfast conferences and teaching demonstrations are scheduled. At the annual dinner Nov. 4, Kenneth McFarland, Ph.D., Topeka, Kan., will present, "3-Dimensional Confidence." Scientific and technical exhibits are arranged, and a ladies' program is planned. For information, write the Interstate Postgraduate Medical Association, P. O. Box 1109, Madison 1, Wis.

CORRECTIONS

Dr. William Herbert Burwig Not Dead.—The report of death of Dr. William Herbert Burwig, of Buffalo, N. Y., which appeared in The Journal, Oct. 3, page 573, was erroneous. William Burwig of Buffalo, reported as dead by the New York State Department of Health, was a naturopath.

Foreign Speakers at Gastroenterology Meeting.—In the Sept. 19 issue of The Journal, page 317, in an item announcing the 24th convention of the American College of Gastroenterology the following should have been listed as foreign speakers: Dr. Xavier de la Riva, Mexico; Dr. Sylvio Markees, Basel, Switzerland; Dr. Octavio Montanez, Mexico; Dr. Jordan T. Propatoridis, Athens, Greece; and Dr. Francisco Puente Pereda, Mexico.

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination.* Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:[*] On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

Arkansas:[*] *Examination and Reciprocity.* Little Rock, Nov. 5-6. Sec., Dr. Joe Verser, Harrisburg.

California: *Oral.* San Francisco, November 14. *Oral and Clinical.* San Francisco, Nov. 15. Sec., Dr. Lous E. Jones, Room 536, 1020 N Street, Sacramento.

Colorado:[*] *Examination.* Denver, Dec. 8-9. *Reciprocity.* Denver, Oct. 14. Exec. Sec., Miss Mary M. McConnell, 715 Republic Bldg., 1612 Tremont Place, Denver 2.

Connecticut:[*] *Examination.* Hartford, Nov. 10-12. Sec. to the Board, Dr. Stanley B. Weld, 160 St. Ronan St., New Haven.

Delaware: *Examination.* Dover, Jan. 12-14. *Endorsement.* Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

District of Columbia:[*] *Examination.* Washington, Dec. 14-15. *Reciprocity.* Washington, Sept. 14. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida:[*] *Examination.* Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Guam: *Subject to Call.* Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination.* Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity.* Boise, Jan. *11, 12, 13.* Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination.* Indianapolis, June 1960. *Reciprocity.* Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:[*] *Examination and Reciprocity.* Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination.* Frankfort, Dec. 14-15. Asst. Sec., Mrs. Ray Wunderlich, 620 South Third St., Louisville 2.

Louisiana: *Examination and Reciprocity.* New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maine: *Examination* and *Reciprocity.* Portland, Nov. 10. Sec., Dr. Stephen A. Cobb, Stanford.

Maryland: *Examination.* Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination.* Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:[*] *Examination.* Jackson, June 1960. *Reciprocity.* Jackson, Dec. 7, Sec., Dr. A. L. Gray, Old Capitol, Jackson.

Nebraska:[*] *Examination.* Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination.* Jan. 19-22. *Reciprocity.* Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New Mexico:[*] *Examination and Reciprocity.* Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination.* Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

North Dakota: *Examination.* Grand Forks, Jan. 6-8. *Reciprocity.* Grand Forks, Jan. 9. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Ohio: *Examination.* Columbus, Dec. 15-17. *Endorsement.* Columbus, Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Pennsylvania: *Examination.* Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

South Carolina: *Examination and Endorsement.* Columbia, Dec. 8. Sec., Dr. H. E. Jervey, Jr., 1329 Blanding St., Columbia.

Texas:[*] *Examination.* Fort Worth, Dec. 3-5. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination.* Salt Lake City, July 6-8. *Reciprocity.* Salt Lake City, Nov. 17. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Virginia: *Reciprocity.* Dec. 1, *Examinations* Dec. 2-4 inclusive, Richmond. Address: Board of Medical Examiners, 631 First St. S. W., Roanoke.

Virgin Islands: *Examination.* Charlotte Amalie, Nov. 12-13. Sec., Dr. Benjamin Nath, Charlotte Amalie, St. Thomas.

Washington:[*] *Examination.* Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination.* Charleston, January. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:[*] *Examination.* Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity.* Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity.* Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

District of Columbia: *Examination.* Washington, Nov. 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida: *Examination.* Gainesville, Nov. 7. Sec., Mr. M. W. Emmel, Box 340, Gainesville.

Kansas: *Examination.* Pittsburg, Nov. 6-7. Sec., Dr. Leon C. Heckert, Kansas State College, Pittsburg.

Rhode Island: *Examination.* Providence, Nov. 18. *Reciprocity.* Providence, Nov. 4. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Dakota: *Examination.* Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Washington: *Examination.* Seattle, Jan. 6-7. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin: *Examination.* Milwaukee, Dec. 5, Madison, Apr. 9, Sec., Mr. Wm. H. Barber, 621 Ranson St., Ripon.

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[*] Basic Science Certificate required.

DEATHS

Abraham, Ernest Guenter Ⓜ New York City; Albertus-Universität Medizinische Fakultät, Konigsberg, *Prussia*, Germany, 1926; fellow of the International College of Surgeons of which he was a vice-president and associate secretary; associated with the Mount Sinai Hospital; died Aug. 17, aged 57.

Adams, Leslie Pleasant, New York City; Emory University School of Medicine, Atlanta, 1931; interned at Nassau Hospital in Mineola, N. Y.; served a residency at the Neurological Institute of New York in New York City, and the Brooklyn State Hospital; certified by the National Board of Medical Examiners; specialist certified by the American Board of Psychiatry and Neurology; associated with the Neurological Institute, Presbyterian Hospital, and Vanderbilt Clinic; died Aug. 4, aged 57.

Adams, Robert Albert, Whitestone, N. Y.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; on the staff of the Flushing (N. Y.) Hospital; died Aug. 3, aged 79.

Alpert, Theodore Nathaniel, Ventura, Calif.; University of Buffalo School of Medicine, 1912; died Aug. 5, aged 72.

Ames, Frederick Daniel Ⓜ Houston, Texas; Harvard Medical School, Boston, 1933; veteran of World War II and won both the Purple Heart and Bronze Star for service in the Southwest Pacific; past-president of the Harris County Pediatrics Society; died in the Veterans Administration Hospital Aug. 12, aged 52.

Asborno, John Nicholas Ⓜ Denver; Creighton University School of Medicine, Omaha, 1956; interned at St. Anthony Hospital; for two years served in the U. S. Air Force; died Aug. 14, aged 28.

Barr, Herman Paul Ⓜ Chicago; Northwestern University Medical School, Chicago, 1921; associated with the South Shore and Little Company of Mary hospitals; died Aug. 22, aged 65.

Bivins, Luther Lee, Copperas Cove, Texas; University of Louisville (Ky.) Medical Department, 1900; at one time city health officer; died in the King's Daughters Hospital in Temple July 25, aged 79.

Bolt, Richard Arthur, Berkeley, Calif.; born in St. Louis March 12, 1880; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1906; served on the faculty of Western Reserve University School of Medicine in Cleveland and the University of California in Berkeley; at one time lecturer at Johns Hopkins University School of Hygiene and Public Health in Baltimore; formerly a director of the Cleveland Child Health Association and chief of the bureau of child hygiene for the department of health of Cleveland; in 1917-1918 director of the United States indemnity program in Peking, China; received two decorations from the Chinese Red Cross for his work during the Chinese Revolution; in 1918-1919 director of the child welfare division of the tuberculosis commission of the American Red Cross in Italy; formerly consultant on maternal and infant hygiene for the U. S. Children's Bureau; served as a member of the White Conference on Child Health and Protection; formerly editor of the child health section of the *Journal of the American Public Health Association;* died in Alta Bates Hospital Aug. 3, aged 79.

Boughton, Geoffrey Allyn Ⓜ Captain, U. S. Army, retired, Larchmont, N. Y.; Boston University School of Medicine, 1954; certified by the National Board of Medical Examiners; interned at the Massachusetts Memorial Hospitals in Boston, where he served a residency; entered the U. S. Army in July, 1957; died in the Walter Reed Army Hospital in Washington, D. C., June 30, aged 30.

Bowen, Robert E. Ⓜ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1903; a division surgeon for Southern Pacific Lines; died in Gonzales Aug. 13, aged 80.

Chamberlain, Herbert Denison Ⓜ McArthur, Ohio; Ohio State University College of Medicine, Columbus, 1933; member of the American Academy of General Practice; veteran of World War I; president of the county board of health; formerly county health officer; died in the Mount Carmel Hospital in Columbus Aug. 10, aged 60.

Cogan, Julius, Reseda, Calif.; Georgetown University School of Medicine, Washington, D. C., 1927; associated with the Olive View (Calif.) Sanatorium; died in the Kaiser Foundation Hospital in Los Angeles Aug. 7, aged 62.

Cole, Norman Brown Ⓜ Baltimore; Harvard Medical School, Boston, 1914; member of the Association of Life Insurance Medical Directors of America; veteran of World War I; medical director and secretary of the Baltimore Life Insurance Company and a member of its board of directors;

Ⓜ Indicates Member of the American Medical Association.

for many years a member of the school board; interested in youth problems, spent much of his leisure time as a scoutmaster, troop committeeman, and was president of the Baltimore Area Council of the scouts; associated with Johns Hopkins Hospital; died in Nantucket, Mass., Aug. 18, aged 73.

Custer, Byron Homer, North Little Rock, Ark.; Kansas City (Mo.) College of Medicine and Surgery, 1926; died Aug. 3, aged 56.

Dean, George Brookhouse, Medford, Ore.; Miami Medical College, Cincinnati, 1898; died in the Rogue Valley Memorial Hospital Aug. 3, aged 86.

De Sautelle, William Thomas Ⓜ Knoxville, Tenn.; Johns Hopkins University School of Medicine, Baltimore, 1911; fellow of the American College of Physicians; served on the staffs of Knoxville General, Fort Sanders Presbyterian, and St. Mary's Memorial hospitals; died Aug. 9, aged 74.

Dorne, Philip Harry Ⓜ Chicago; Northwestern University Medical School, Chicago, 1914; member of the American Academy of Dermatology and Syphilology; staff member at Alexian Brothers Hospital; veteran of World War I; died Aug. 20, aged 69.

Duggan, Henrietta Hagan Ⓜ San Francisco, Calif.; University of California School of Medicine, San Francisco, 1903; served on the staffs of the University of California, Children's, and St. Mary's hospitals; died Aug. 7, aged 78.

Dunbar, Helen Flanders Ⓜ New York City; born in Chicago May 14, 1902; Yale University School of Medicine, New Haven, Conn., 1930; specialist certified by the American Board of Psychiatry and Neurology; certified by the National Board of Medical Examiners; fellow of the New York Academy of Medicine, American Psychiatric Association, of which she was secretary treasurer, 1939-1940, American Geriatrics Society, International Association of Gerontology, and the New York Academy of Science; member of the American Association for the Advancement of Science, New York Society of Clinical Psychiatry, American Psychoanalytic Association, treasurer from 1942 to 1945, American Psychopathological Association, serving as vice-president from 1942 to 1945, Association for Research in Nervous and Mental Diseases, International Psychoanalytic Association, National Committee on Alcoholism, National Safety Council, New York State Academy of General Practice, World Medical Association, American Orthopsychiatric Association, American Psychosomatic Society, American Committee for World Federation for Mental Health, and Greenwich Medical Society; served on the faculty of Columbia University College of Physicians and Surgeons, and from 1941 to 1949 instructor at New York Psychoanalytic Institute; at various times associated with the Bellevue, Presbyterian, and Greenwich (Conn.) hospitals, and the Vanderbilt Clinic; editor in chief emeritus of *Psychosomatic Medicine,* of which she was editor in chief from 1938 to 1947; collaborating editor from 1938 to 1940 and editor, 1939-1940, *Psychoanalytic Quarterly;* author of "Symbolism in Medieval Thought," "Emotions and Bodily Changes," "Psychosomatic Diagnosis," "Your Child's Mind and Body," "Mind and Body," and "Psychiatry in the Medical Specialties"; died Aug. 21, aged 57.

Faucett, Robert Lynn Ⓜ Rochester, Minn.; born in Independence, Mo., April 6, 1916; University of Kansas School of Medicine, Kansas City, Mo., 1944; interned and was resident in pediatrics at the University of Kansas Hospitals in Kansas City, Kan., from 1944 to 1946; in December, 1946, commissioned a senior assistant surgeon in the U. S. Public Health Service, assigned to the USPHS Hospital in Lexington, Ky.; in July, 1948, was assigned by the USPHS to the department of psychiatry at the University of Minnesota for graduate study in pediatric psychiatry; came to Rochester a year later as a special worker with the former Rochester Child Health Institute; from January to June, 1950, a fellow in neurology and psychiatry in the Mayo Foundation; in March of that year became a part-time psychiatric consultant at the Counselling Clinic of the Rochester–Olmsted County Public Health Center, and on July 1 was appointed director of the Counselling Clinic for a term of six months; left Rochester in January, 1951, to become director of the Prince Georges County Health Clinic at the University of Maryland in College Park, Md.; also continued psychoanalysis studies at the Washington Psychoanalytic Institute in graduate training; returned to Rochester on July 1, 1953, as a consultant in psychiatry in the Mayo Clinic; appointed instructor in psychiatry in the Mayo Foundation, Graduate School, University of Minnesota, in 1955, and was advanced to the grade of assistant professor in 1959; in 1957 was a member of the faculty at the first workshop on psychological problems of pastoral care at St. John's University in Collegeville, Minn.; specialist certified by the American Board of Psychiatry and Neurology; member of the Minnesota Psychiatric Society, American Psychosomatic Society, the Society of the Sigma Xi and the Alumni Association of the Mayo Foundation; fellow of the American Psychiatric Association; died Aug. 5, aged 43.

Glodt, Milton, Boston; Universität Basel Medizinische Fakultät, Switzerland, 1936; died in Nantucket, Mass., Aug. 14, aged 56.

Goodman, Thomas L. Ⓜ Fort Worth, Texas; Fort Worth School of Medicine, Medical Department of Texas Christian University, 1913; past-president of the Tarrant County Medical Society; served on the staffs of City and County Hospital and St. Joseph's Hospital; died Aug. 4, aged 77.

Graham, James Jahue, Marion, S. C.; Meharry Medical College, Nashville, Tenn., 1928; died Aug. 17, aged 72.

Gregg, Arthur William Ⓜ Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1909; member of the senior surgical staff, Walther Memorial Hospital; died Aug. 26, aged 76.

Haining, Lois Nicolini, San Francisco; Stanford University School of Medicine, San Francisco, 1956; interned at the Los Angeles County Hospital; served a residency at the Veterans Administration Hospital in Iowa City, Iowa; died in Pacifica July 28, aged 28.

Hart, George H., Davis, Calif.; George Washington University School of Medicine, Washington, D. C., 1908; member of the Endocrine Society; dean emeritus, University of California School of Veterinary Medicine; died in Woodland, Aug. 2, aged 75.

Harvey, Fredric Everett Ⓜ Minneapolis, Kan.; Kansas City (Mo.) Medical College, 1905; veteran of World War I; during World War II Selective Service examiner; served as health officer of Ottawa County; formerly on the staffs of St. John's and Asbury hospitals in Salina; died in the Concordia (Kan.) Hospital Aug. 6, aged 77.

Hass, Julius Ⓜ New York City; Medizinische Fakultät der Universität, Vienna, Austria, 1910; member of the American Academy of Orthopaedic Surgeons; fellow of the International College of Surgeons; associated with the Hospital for Special Surgery, Montefiore Hospital, Madison Avenue Hospital, and the Manhattan General Hospital; died Aug. 17, aged 76.

Hatton, Edward Howard, Evanston, Ill.; Rush Medical College, Chicago, 1912; for many years professor of pathology at Northwestern University Dental School; served on the faculty of his alma mater from 1917 to 1919; coroner's physician for Cook County from 1916 to 1923; past-president and secretary-treasurer of the International Association for Dental Research; died in the Evanston Hospital Aug. 15, aged 83.

Haury, Paul Gerhardt Ⓜ Lewiston, Idaho; Northwestern University Medical School, Chicago, 1929; fellow of the American College of Surgeons; past-president of the North Idaho Medical Society; veteran of World War II; formerly member of the city council; on the staff of St. Joseph's Hospital; died Aug. 9, aged 59.

Hazzard, Lawrence Rosseau, Portsmouth, N. H.; University of Kansas School of Medicine, Kansas City, Kan., 1918; fellow of the American College of Surgeons; past-president of the New Hampshire Surgical Club; veteran of World War I; associated with the Portsmouth Hospital, where he died Aug. 10, aged 70.

Healy, Merritt Wood Ⓜ Norfolk, Va.; University College of Medicine, Richmond, 1906; served overseas during World War I; for many years surgeon for the Norfolk Shipbuilding and Drydock Corporation; died Aug. 14, aged 76.

Hill, Irvin Bartle Ⓜ Salem, Ore.; University of Oregon Medical School, Portland, 1939; interned at the Good Samaritan Hospital in Portland; served a residency at the Oregon State Hospital; member of the American Psychiatric Association; served as vice-president of the American Association of Mental Deficiency; on the faculty of his alma mater; administrator, Oregon Fairview Home; died Aug. 17, aged 44.

Hinton, William Augustus Ⓜ Boston; born in Chicago Dec. 15, 1883; Harvard Medical School, Boston, 1912; the first Negro ever awarded a professorship at Harvard, where in 1949 he was appointed clinical professor of bacteriology and immunology, and held teaching positions for many years; from 1919 to 1953 lecturer at Simmons College; chief of clinical laboratories of the Boston Dispensary from 1916 to 1952; served as chief of the laboratories of the Boston Floating Hospital; a director of the Committee on Research and Syphilis, Inc.; for many years a special consultant to the U. S. Public Health Service and consultant to the Massachusetts School for Crippled Children; on Dec. 31, 1953, retired after 38½ years of service as director of the Wassermann Laboratory of the Massachusetts Department of Public Health, and Governor Christian A. Herter commended him "both as a noted scientist and faithful servant of the Commonwealth"; devised the Hinton Test for the detection of syphilis, used by the U. S. Armed Forces, hospitals, clinics, and public health laboratories throughout the world; with the assistance of Dr. John A. V. Davies, of Children's Hospital, also developed the Davies–Hinton test, a test on spinal fluids for the detection of syphilis in the nervous system; served as a member of the American Society of Clinical Pathologists, the Society of American Bacteriologists, the American Association for the Advancement of Science, and the American Public Health Association; author of "Syphilis and Its Treatment" published in 1936; died Aug. 8, aged 75.

Hitchcock, John Phinizy Ⓜ Augusta, Ga.; Medical College of Georgia, Augusta, 1936; interned at the University Hospital, where he served a residency; member of the Southeastern Surgical Congress; fellow of the American College of Surgeons; veteran of World War II; on the staffs of St. Joseph's Hospital and the University Hospital, where he died Aug. 7, aged 48.

Horwitz, Ellis Berry Ⓜ Philadelphia; Medico-Chirurgical College of Philadelphia, 1915; served during World War II; died in the Temple University Hospital Aug. 17, aged 67.

Houghton, Montafix Wilson Ⓜ Providence, R. I.; George Washington University School of Medicine, Washington, D. C., 1904; veteran of World War I; retired acting assistant surgeon in the U. S. Public Health Service; associated with the Roger Williams General Hospital; died Aug. 9, aged 79.

Houston, David H. Ⓜ Seattle; Queen's University Faculty of Medicine, Kingston, Ont., Canada, 1903; past-president of the Washington State Obstetrical Association, King County Medical Society, and Washington State Golfing Association; a past-president of the American Medical Golfing Association, of which he was permanent chairman; a trustee, formerly chief of obstetrics, and an honorary staff member, Virginia Mason Hospital; served as chief of obstetrics at King County Hospital and on the staff of the Doctors Hospital; died Aug. 4, aged 78.

Hutnick, Stephen Emanuel, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1920; died July 2, aged 64.

Jackson, Arthur Husted, Watkins Glen, N. Y.; Syracuse University College of Medicine, 1904; for many years county coroner; served as a member and president of the board of education of Odessa and Watkins Glen; associated with the Willard (N. Y.) State Hospital and the Schuyler Hospital in Montour Falls, where he died Aug. 14, aged 80.

James, Francis Marshall Jr. Ⓜ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1930; associated with the Memorial Hospital, where he died Aug. 7, aged 55.

Janss, Edwin, Los Angeles; Northwestern University Medical School, Chicago, 1903; veteran of World War I; died in St. John's Hospital, Santa Monica, Aug. 19, aged 77.

Johnson, Cecil Emerson Ⓜ Rensselaer, Ind.; Northwestern University Medical School, Chicago, 1910; veteran of World War I; served as county health officer; died in St. Elizabeth Hospital, Lafayette Aug. 2, aged 70.

Jones, Ralph Northrup, Whitefield, N. H.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1931; veteran of World War I; associated with the Morrison Hospital, where he died Aug. 6, aged 61.

Kaufman, Charles, New London, Conn.; Jefferson Medical College of Philadelphia, 1919; fellow of the American College of Surgeons; served on the staff of the Lawrence and Memorial Hospitals; died Aug. 8, aged 64.

Keppler, Charles Jr., Mount Shasta, Calif.; University of Virginia Department of Medicine, Charlottesville, 1930; also a graduate in pharmacy; died Aug. 14, aged 55.

Kimble, James Norman Ⓜ Takoma Park, Md.; College of Medical Evangelists, Loma Linda and Los Angeles, 1933; specialist certified by the American Board of Radiology, Inc.; member of the American College of Radiology; past-president of the Montgomery County Medical Society; interned, and for many years director of radiology at the Washington Sanitarium and Hospital, where he died Aug. 13, aged 73.

Kirkpatrick, Milton Barnes Ⓜ Montgomery, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; for many years coroner of Montgomery County; associated with the Fitts Hill Hospital and St. Margaret's Hospital, where he died Aug. 8, aged 88.

Kirkwood, Elmer Earle Ⓜ Youngstown, Ohio; St. Louis University School of Medicine, 1919; member of the American College of Chest Physicians and past-president of the Ohio Chapter; member of the American Academy of General Practice; for many years associated with the Mahoning Tuberculosis Sanatorium, of which he was medical director; served on the staff of the Cleveland Municipal Tuberculosis Sanatorium in Warrenville, Ohio; died in the North Side unit of the Youngstown Hospital Aug. 14, age 65.

Kirwin, Thomas Joseph Ⓜ New York City; born in Scranton, Pa., Aug. 31, 1889; Tulane University School of Medicine, New Orleans, 1916; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons and the International College of Surgeons; served on the faculty as professor of urology at New York Medical College, Flower and Fifth Avenue Hospitals; veteran of World War I; associated with the Flower and Fifth Avenue, Metropolitan, Bird S. Coler, and New York hospitals, New York City, Coney Island Hospital, Brooklyn, Benedictine Hospital, Kingston, N. Y., Monmouth Memorial Hospital in Long Branch, Passaic (N. J.) Hospital, and South Nassau Communities Hospital in Rockville Centre; joint author of "Textbook of Urology," "Urology for Nurses," and two volumes of "Clinical Urology"; died in the New York Hospital Aug. 18, aged 69.

Kraus, Karl Joseph, Las Vegas, Nev.; University of Cincinnati College of Medicine, 1934; veteran of World War II; died Aug. 5, aged 51.

Laughlin, Judson, Clarion, Iowa; Central Medical College of St. Joseph, Mo., 1896; associated with the Clarion Memorial Hospital, where he died July 21, aged 91.

Little, William Bracey, Plaquemine, La.; Meharry Medical College, Nashville, Tenn., 1912; died Aug. 6, aged 79.

McDevitt, Daniel Robert Ⓢ Indianapolis; Indiana University School of Medicine, Indianapolis, 1923; member of the American Academy of General Practice; associated with St. Vincent's, Methodist, and St. Francis hospitals; died Aug. 15, aged 62.

McKinstry, Herbert Sydney Ⓢ Kennett Square, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1917; member of the American Academy of General Practice; at one time president of the Chester County Medical Society; served overseas during World War I; associated with the West Chester (Pa.) Memorial Hospital; on the courtesy staff of Chester County Hospital in West Chester, and the Memorial Hospital, Wilmington, Del., where he died Aug. 7, aged 70.

McLaughlin, James Francis Ⓢ Adams, Mass.; Tufts College Medical School, Boston, 1919; veteran of World War I; for many years member of the board of health; formerly medical consultant for the Adams Welfare Department; past-president of the Adams Anti-Tuberculosis Association; associated with the Plunkett Memorial Hospital; died Aug. 11, aged 64.

McNaught, James Bernard Ⓢ Denver; born in Girard, Kan., July 11, 1894; Stanford University School of Medicine, San Francisco, 1931; served as head of the department of pathology at the University of Colorado School of Medicine, where he was professor of pathology; instructor in bacteriology at the University of Kansas, Lawrence, from 1919 to 1921; joined the faculty of his alma mater as an assistant in pathology, subsequently becoming instructor, assistant professor, and associate professor of pathology; in 1934-1935 exchange instructor of pathology at the University of Rochester (N. Y.) School of Medicine and Dentistry; from 1937 to 1945 director and pathologist at the Palo Alto (Calif.) Hospital; veteran of World War I; since 1948 consultant to Atomic Energy Commission, Division of Biology and Medicine; expert consultant to Surgeon General, U. S. Army, since 1946; consultant in pathology to Surgeon General of the U. S. Air Force since 1952; area consultant in pathology, St. Louis Medical Area, Veterans Administration since 1946; member of the scientific advisory board of consultants to Armed Forces Institute of Pathology; specialist certified by the American Board of Pathology, of which he was a trustee from 1944 to 1956, and president from 1953 to 1955; member of the American Association of Pathologists and Bacteriologists, of which he was councilor in 1949 and later president; founding fellow and past-governor of the College of American Pathologists; member and past-president of the American Society of Clinical Pathologists and in 1957 received its Certificate of Highest Merit; formerly councilor, vice-president, and president of the International Association of Medical Museums; past-president of the International Academy of Pathology; charter member of the American Physicians Art Association; member of the American Society for Experimental Pathology, American Association for the Advancement of Science, American Society of Tropical Medicine, American Society for Parasitology, Federation of American Societies for Experimental Biology, Society for Experimental Biology and Medicine, Alpha Kappa Kappa, Alpha Omega Alpha, Phi Delta Kappa, and Sigma Xi; died in the Veterans Administration Hospital, Albuquerque, N. M., Aug. 7, aged 65.

Mason, Charles Leonard Ⓢ Durango, Colo.; University of Colorado School of Medicine, Denver, 1932; interned at the Hillman Hospital in Birmingham, Ala., and the St. Joseph's Hospital in Denver; veteran of World War II; associated with the Mercy Hospital; died Aug. 5, aged 52.

May, Murray Morris, Brooklyn; Universität Bern Medizinische Fakultät, Switzerland, 1936; veteran of World War II; died June 6, aged 52.

Mattson, James Marshall Ⓢ Tacoma, Wash.; University of Pennsylvania School of Medicine, Philadelphia, 1939; interned at the Scott and White Hospital in Temple, Texas, where he served a residency; associated with the Tacoma General, St. Josephs, Medical Arts, and Doctors hospitals; died Aug. 1, aged 47.

Miears, Claude H. Ⓢ Austin, Texas; University of Oklahoma School of Medicine, Oklahoma City, 1925; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; associated with the Brackenridge, Seton, and Holy Cross hospitals; on the honorary staff of St. David's Hospital; died Aug. 5, aged 64.

Miller, Isidore Ⓢ New York City; University and Bellevue Hospital Medical College, New York City, 1911; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the American College of Surgeons; veteran of World War I; associated with the New York Eye and Ear Infirmary and the Jewish Memorial Hospital; died Aug. 12, aged 75.

O'Connor, Dermot Fenton Ⓢ Syosset, N. Y.; University College, Dublin, Ireland, 1941; interned at the Doctors Hospital in New York City; associated with the Meadowbrook Hospital in Hempstead and the Community Hospital in Glen Cove, where he died July 21, aged 41.

Pennington, Alfred William Ⓢ Newark, Del.; Medical College of Virginia, Richmond, 1929; specialist certified by the American Board of Internal

Medicine; fellow of the American Academy of Occupational Medicine and the Industrial Medical Association; associated with the medical division of E. I. DuPont de Nemours Company; died Aug. 9, aged 56.

Phillips, Lawrence Curtis, Pensacola, Fla.; Hering Medical College, Chicago, 1903; died Aug. 5, aged 86.

Poirier, George Henri Ⓜ Boston; Tufts College Medical School, Boston, 1910; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology and the American Laryngological, Rhinological and Otological Society; veteran of World War I; associated with the Massachusetts Eye and Ear Infirmary; died Aug. 8, aged 73.

Potter, Caroline Colver, East Lansing, Mich.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1900; died Aug. 4, aged 81.

Roemer, Thomas Jacques Ⓜ Portland, Ore.; State University of Iowa College of Medicine, Iowa City, 1930; associated with the St. Vincent's Hospital, Providence Hospital, and the Good Samaritan Hospital, where he died Aug. 1, aged 58.

Saxon, Robert Lee Ⓜ Little Rock, Ark; University of Nashville (Tenn.) Medical Department, 1900; past-president of the Pulaski County Medical Society; formerly on the faculty of the University of Arkansas School of Medicine; served on the staffs of the St. Vincent Infirmary and the Arkansas Baptist Hospital; died in the Methodist Hospital in Houston, Texas, Aug. 9, aged 85.

Schofield, James Dobson Ⓜ Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1902; specialist certified by the American Board of Surgery and the American Board of Proctology; member of the American Proctologic Society; fellow of the American College of Surgeons; veteran of World War I; associated with Hahnemann Medical College and Hospital and the St. Luke's and Children's Medical Center; died at his home in Wynnewood, Pa., Aug. 9, aged 80.

Smith, Ellis Jacob Ⓜ Cincinnati; Eclectic Medical College, Cincinnati, 1925; served on the staff of St. Francis Hospital; died Aug. 8, aged 62.

Sutherland, Justus, Oshkosh, Wis.; Milwaukee Medical College, 1900; veteran of World War I; served on the staff of the Veterans Administration Hospital in Wood; died in the Mercy Hospital July 26, aged 83.

Symonds, Cleon Walter Ⓜ Redlands, Calif.; Harvard Medical School, Boston, 1910; veteran of World War I; fellow of the International College of Surgeons; died in the Loma Linda (Calif.) Sanitarium and Hospital July 26, aged 75.

Thomson, Robert Robertson, Berkeley, Calif.; University of California School of Medicine, San Francisco, 1928; served on the staff of the Ernest V. Cowell Memorial Hospital; died July 29, aged 71.

Ulfelder, Sidney, Mexico City, D. F., Mexico; Columbia University College of Physicians and Surgeons, New York City, 1896; associated with the American British Consulate Hospital; died in McLean, Va., Aug. 9, aged 84.

Vary, Edwin Phelps Ⓜ Flint, Mich.; University of Michigan School of Medicine, Ann Arbor, 1930; specialist certified by the American Board of Surgery; fellow of the American College of Surgeons; veteran of World War II; associated with the McLaren General, Hurley, and St. Joseph hospitals; died Aug. 2, aged 54.

Wadhams, Sanford H. Ⓜ Colonel, U. S. Army, retired, Torrington, Conn.; Yale University School of Medicine, New Haven, 1896; entered the Army in 1900 and retired July 16, 1921; veteran of World War I; fellow of the American College of Surgeons; died in the Charlotte Hungerford Hospital June 14, aged 85.

Watson, Herbert Shirley, Earle, Ark.; University of Tennessee College of Medicine, Memphis, 1916; veteran of World War I; died in the Veterans Administration Hospital in Memphis, Tenn., July 29, aged 67.

Wheeler, James Hartwick Ⓜ Henderson, N. C.; Jefferson Medical College of Philadelphia, 1918; past-president of the Vance County Medical Society; for many years served on the board of education; a director of the Home Building and Loan Association; formerly vice-president of the Commercial and Industrial Bank; past-president of the Henderson Rotary Club; one of the founders and on the staff since its inception, Maria Parham Hospital, where he died July 22, aged 68.

Woodburne, Arthur Wellesley, Tampa, Fla.; University of Western Ontario Faculty of Medicine, London, Ont., Canada, 1898; fellow of the American College of Surgeons; formerly practiced in Entrican and Hastings, Mich.; once a medical missionary in India; died Aug. 1, aged 84.

Zessin, Elmer Theodore Paul Ⓜ Galesburg, Ill.; Chicago College of Medicine and Surgery, 1914; associated with Galesburg Cottage Hospital and the St. Mary's Hospital, where he died July 27, aged 73.

Zonis, Jonathan Ⓜ Boston; Tufts College Medical School, Boston, 1924; member of the American College of Allergists; served on the faculty of his alma mater; associated with the Mount Sinai Hospital, Jewish Memorial Hospital, and the Beth Israel Hospital, where he died July 18, aged 64.

FOREIGN LETTERS

BRAZIL

Brazilian Trypanosomiasis.—Drs. Jatene and Jacomo, of Uberaba, Minas, studied the problem of transmitting trypanosomiasis through blood transfusion (*Revista goiana de medicina,* March, 1959). They found that the percentage of donors in São Paulo City with a positive Machado Guerreiro reaction (indicative of trypanosomiasis) was higher than that for those with a positive Wassermann test. In the city of Uberaba 15% of the blood donors gave a positive Machado Guerreiro reaction. Some authors have suggested that the blood from donors with positive Machado Guerreiro tests should be sterilized in vitro. Jatene and Jacomo recommended that any blood to be transfused in areas with a high incidence of trypanosomiasis be treated with gentian violet as the only effective preventive measure.

Dr. C. C. Porto, of Belo Horizonte, Minas, in the same issue reported on his electrocardiographic studies of 78 apparently healthy children. Of these, 17 showed a positive Machado Guerreiro reaction, 58 were negative, and in 3 the test was not conclusive. Ventricular premature beats and marked bradycardia in the group with negative Machado Guerreiro reactions made him suspect the possibility of trypanosomiasis and the development of a positive reaction in the future. In the group with a positive reaction, one child had a right bundle-branch block and one had a first degree atrioventricular block. He concluded that these abnormal electrocardiographic findings probably represented the first step in the development of trypanosomiasis and that it is desirable to follow up these patients for a long time.

FRANCE

Marrow Transfusions for Accidental Irradiation.—H. Jammet and co-workers made a further study of the six Yugoslavian scientists who received accidental irradiation and were treated in Paris (*Revue française d'études cliniques et biologiques,* vol. 4, March, 1959). These scientists, five men and one woman, were classified in three categories, according to the degree of irradiation received. One received 1,000 r; four received from 600 to 999 r; and one received 400 r. Warning symptoms such as asthenia, psychic depression, anorexia, nausea, vomiting, sweating, and paresthesia of the upper limbs appeared during the hour after the accident. The least irradiated of these patients had no vomiting; the most irradiated, who later died, besides the symptoms listed above, also had diarrhea.

In the latent period (three weeks) the patients' general condition was comparatively satisfactory in contrast with the course of the hematological, cutaneous, and visceral disorders. Erythema appeared on the first day, accompanied by conjunctivitis. Epilation of the scalp and beard started on the 14th day. Dryness of the skin and subsequent scaling occurred in the subject who received the largest dose. The hemorrhagic disorders were in the forms of epistaxis, gingival bleeding, hematemesis, and, in the woman, menorrhagia. Hematological disorders were immediate leukocytosis (9,000 to 11,000 cells per cubic millimeter) and ensuing lymphopenia. In the latent period there was a gradual decrease in the blood elements. This decrease became more and more marked as it involved first the erythrocytes, then the lymphocytes, thrombocytes, and granulocytes. There was a sharp decrease in lymphocytes during the first five days, with subsequent fluctuations.

The reticulocytes practically disappeared after the first few days, and a reticulocytic crisis occurred at the end of the second week. Then there was a critical period of four to seven weeks, with deterioration of the general condition and clinical findings suggesting typhus except in the subject who received the smallest dose. The nausea recurred, with profuse sweating and diminished diuresis. This critical period was hematologically characterized by an almost total medullary aplasia. The number of neutrophils and of thrombocytes per cubic millimeter fell, respectively, to below 50 and to 30,000. The erythrocyte counts varied from 1,400,000 to 3,000,000.

G. Mathé and co-workers in the same issue reviewed the treatment given to these patients. It started with transfusion of whole blood, platelets, and gamma globulin and administration of antibiotics. In view of the aggravation of the condition, a grafting of embryonic myeloid cells was attempted. The patient who was most heavily irradiated was given a large transfusion of cells from the spleen and liver of a premature infant who had died a few hours after birth. Ten days later his condition deteriorated with the onset of an intestinal syndrome and pain in the right iliac fossa, due to a thrombus. A transfusion of medullary cells from a volunteer donor was then performed. Four days later a rapid increase in blood

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The items in these letters are contributed by regular correspondents in the various foreign countries.

cells was observed, but the intestinal signs were aggravated and the patient's condition was further complicated by anuria and acute renal insufficiency. This patient died from a massive respiratory hemorrhage in spite of an extrarenal dialysis with an artificial kidney.

In view of the aggravation in the hematological condition of the four other heavily irradiated patients, an intravenous injection of marrow from volunteer donors was performed. Each patient received 180 to 300 cc. and a large transfusion of cells. The hematological and clinical conditions took a favorable course. A rapid increase in the reticulocyte, erythrocyte, granulocyte, and platelet counts occurred. The temperature dropped to normal a few days after the marrow was given with a noticeable improvement in the general condition, disappearance of the typhus-like findings, increase in appetite, and gain of weight. Through the study of the blood group phenotypes, by the method of differential agglutination, it was possible to establish the respective percentages of erythrocytes belonging to the donors' phenotypes and of those carrying the patients' own antigens. The curves of the donors' antigens rose to a maximum, then dropped, about one month after the marrow transfusion. The correction of the anemia seemed to be entirely related to the erythrocytic production from the graft.

Some weeks later there were slight oscillations in the granulocytic and thrombocytic curves (the granulocyte count oscillated between 4,000 and 2,000, and the thrombocyte count, between 200,000 and 120,000). This mild disorder was probably due to the replacement, by the patients' own cells, of those produced by the original cells from the donors. The leukocytic and thrombocytic production had had the same origin for one month, i. e., they had originated from the grafted marrow, then they had been destroyed. As their life is much shorter than that of the erythrocytes, the number of leukocytes and thrombocytes replaced must have been much higher than the number of erythrocytes. As to the prognosis, the authors expected hematological fluctuations, spermatogenic abnormalities, and persistence of asthenia for a few months. The probability of induced leukemia or other forms of cancer has increased for these subjects.

GERMANY

Iproniazid for Mental Disturbances.—H. P. Hoheisel (*Medizinische,* no. 12, p. 537, 1959) stated that iproniazid, which was originally developed as a tuberculostatic, aroused the interest of psychiatrists when patients treated with it showed a marked improvement in their contact with reality. Further studies showed the drug to be a potent monoamino-oxydase inhibitor and to cause an accumulation of serotonin and catecholamines in the brain. A series of 74 patients was treated with iproniazid for a long enough period to warrant evaluation. Of these 41 had depressive conditions and 33 had obsessive neuroses. In the depressive group 21 were having their first attack. Results of treatment were surprisingly good in almost all patients. Only three depressive patients were not benefited in spite of treatment being continued for six weeks or more. Side-effects, such as constipation, dryness of the mouth, paresthesias, and exaggerated reflexes, were not observed, although they had been reported by others after treatment with iproniazid. The first noticeable results were seen after only 8 to 12 days. After this period the patients were always relaxed and tractable. After 14 to 20 days of treatment most patients were psychically normal and additional shock or sleep treatment was not required.

In the patients with obsessive neuroses there were more failures. Treatment was started with small gradually increasing doses (50 mg. for five days, then 100 mg. for three or four weeks). Caution is required in iproniazid treatment of patients with renal or hepatic disease and in such patients function tests of the diseased organ are necessary at regular intervals. When an improvement of the psychic condition was manifest, the dose was reduced to 75 mg., then to 50 mg., and eventually to a maintenance dose of 25 mg. for 14 days. The patients should be warned that alcohol intolerance exists during treatment. Side-effects were rare. Three patients developed hepatitis during treatment.

Puerperal Mastitis.—H. Schmidt-Matthiessen (*Landarzt* 35:437, 1959) stated that reports of mastitis should differentiate between patients delivered in the home and those delivered in the hospital as well as between early and late inflammation of the lactating breast. Figures of the incidence of mastitis are contradictory, but reports of a statistically significant increase are unanimous. It occurs in 0.98 to 4.5% of all puerperal patients irrespective of the place of delivery and it is more frequent in uniparas than in multiparas. The inflammation usually occurs five to nine days post partum. Late mastitis mainly affects women who gave birth in the hospital. The women have returned to their homes in many cases when the first signs of the infection become manifest. This may be the reason why late mastitis usually takes a severer course than early mastitis. The women, having just returned from the hospital, do not consult their doctors at first and therefore come for treatment only in a late stage of the condition.

About 96% of patients with early mastitis can be treated by purely conservative measures. The tendency to abscess formation is negligible. If mastitis following hospital delivery leads to tissue breakdown, Staphylococcus aureus hemolyticus is found in the pus in 80 to 95% of the patients. These organisms are usually resistant to penicillin, streptomycin, and sulfonamides, and it is necessary to use a broad-spectrum antibiotic. In patients delivered at home Staphylococcus albus is also frequently found. In these patients both organisms are usually sensitive to chemotherapeutic agents, thus rendering conservative treatment much easier. The mechanism of infection occurs when pathogens, which may be found in the nasopharynx of the child from about the fifth day on, enter the breast through small fissures during nursing. Prophylactic measures to be observed are good ventilation of rooms, hygienic care of the nipples, wearing of face masks for mothers and nursing personnel, and disinfection of hands.

In its early stage the infection can often be controlled by x-ray treatment. After pumping the breast 80 to 100 r are given and this treatment, if necessary, may be repeated on the following day. If the symptoms have disappeared by the second day, the breast is emptied again on the third day, and nursing carefully resumed on the fourth day. Patients with late mastitis are given antibiotics in addition. Should the local symptoms not subside, incision and drainage is necessary. The child is not nursed then because of the danger of transmitting the infection with the milk. Phenobarbital, diethyldioxystilbene-dipropionate, and estrin, together with restriction of fluid intake, usually make it possible to control the initial milk flow.

Spermiogenetic Infantilism.—O. Hornstein (*Klin. Wchnschr.* 37:105, 1959) stated that partial insufficiency of the anterior lobe of the hypophysis produces a variety of symptoms, according to the degree and time of dysfunction. The gonadotropic hormones are usually lacking at first. Deficiency of both gonadotropic factors, interstitial cell stimulating hormone and follicle stimulating hormone (ICSH and FSH), as a rule, occur simultaneously. This gives rise to the so-called hypogonadotropic hypogenitalism. Clinical observations are, however, suggestive of an isolated deficiency of FSH, too, which causes a syndrome termed "fertile eunuchoidism," since in it true spermiogenesis is preserved while secondary sex characteristics are not developed. The opposite condition—isolated deficiency of ICSH—has not been observed.

The following case, therefore, deserves special attention: A 32-year-old man came for consultation because his marriage had been sterile. He was of somewhat hypovirile but not eunuchoid build. His voice changed at 20 and at that time he first shaved. He married at 26 years of age. His libido was normal. Examination revealed a light beard growth and feminine distribution of pubic hair. His testes were only cherry-size and soft. No sperms were present in the spermiogram. Gonadotropin and 17-ketosteroid levels were low. A testicular biopsy revealed, apart from a well-developed interstitium with clusters of Leydig's cells, only tubules of infantile appearance with indistinct cellular structure, no sperm cells or mature precursors. This appeared to be a case of dissociated secondary hypogenitalism, which may be explained by the absence of FSH stimulation of the tubules since puberty. In this case it represents the opposite condition to "fertile eunuchoidism," the secondary sex characteristics having been developed by the stimulation of interstitial cells, but spermiogenesis not having been initiated because of FSH deficiency.

Malformations in Newborn Infants.—H. Oster (*Kinderärztl. Praxis* 27:28, 1959) stressed the importance of studying the incidence of malformations of newborn infants in the last two decades in order to determine whether as a result of atomic explosions the incidence of malformations and anomalies in neonates has been increasing. The comprehensive material presented by the author showed no increase in the incidence of malformations for the period 1939 to 1953 compared with the period 1954 to 1958.

INDIA

Chlorpromazine for Tetanus.—B. J. Vakil and coworkers (*Journal of Association of Physicians of India*, vol. 7, July, 1959) treated 259 patients who had tetanus with chlorpromazine in addition to the routine standard treatment. Chlorpromazine was given only to those whose spasms were severe, frequent, and uncontrollable by the routine treatment. Another 81 patients with mild symptoms were controlled with sedatives only. Another group of patients admitted prior to these, and who received only the usual treatment, served as controls. The standard treatment consisted of local treatment of the wound and administration of the antitoxins, antibiotics, and sedatives. Cortisone or its derivatives were occasionally used to relieve allergy or anaphylaxis and mephenesin was sometimes given to facilitate feeding. Tracheotomy was performed on three patients. The dose of chlorpromazine was adjusted according to requirements but a total dose of 1 Gm. in 24 hours was seldom exceeded. The method of choice for administering this drug was the intravenous drip. The largest daily dose used was 1.5 Gm. in an adult. The longest period of administration was 12 days, with the drug being discontinued when the spasms were reduced in intensity and could be controlled by sedatives only.

The case fatality rate with this treatment was 25% while in the control group it was 35%. The authors found the results with chlorpromazine gratifying in the control of spasms and rigidity. Hypertonia and rigidity were reduced in most patients but rarely were abolished completely. Symptoms of a few patients were, however, completely resistant to the drug even in large doses. Thus, of the 259 patients, 221 showed a favorable response, and 15 died of glottic spasms while the drip was being administered. Neonates and children responded poorly to the drug. The patients so treated were on the whole, relaxed, cheerful, and conscious and feeding was much simpler as most could be fed orally. Coma and respiratory depressions were not serious problems as they were in the control group. No major toxic reaction occurred. In this series eight patients had cephalic tetanus, which is a type well known for its poor prognosis. With chlorpromazine seven of the eight survived. None of the neonates in the control series survived while in the present study 2 of 17 were saved.

Serum Amylase in Mumps.—N. P. Misra *(Journal of the Association of Physicians of India,* vol. 7, July, 1959) determined the serum amylase level in 17 patients with mumps. The normal range was determined in 100 normal subjects. The level was elevated in all the patients. The highest level was observed in the first week of illness except in one patient. In most patients, the level returned to normal by the end of the second week, coinciding with the clinical remission of the disease. A close relation was noticed between the severity of the clinical condition and the serum amylase level. It was also highest in patients whose swelling was most prominent and higher in those with bilateral than in those with unilateral involvement. Development of orchitis, unilateral or bilateral, did not influence the level. The serum amlyase level elevation in patients with mumps was thus a function of the disease associated with parotitis alone. This finding may be used to differentiate mumps from swelling of the face due to other causes such as an impacted molar, bull-neck following diphtheria, lymphadenitis, cellulitis, and fracture-dislocation of the mandible.

C-Reactive Proteins.—P. M. Chaphekar *(Journal of Postgraduate Medicine,* vol. 5, July, 1959) stated that the C-reactive protein (CRP) level reflects the activity of pneumococcic pneumonia and it disappears promptly when the progress of the disease is arrested. The test is of greater help in assessing prognosis than in making a diagnosis. The author studied the CRP level in diseases of the liver to find out whether it would help in judging the activity of the destructive and inflammatory processes associated with viral hepatitis and cirrhosis. Estimations of the sedimentation rate were carried out simultaneously. In 31 normal subjects of both sexes from 1 to 40 years old the test for CRP was uniformly negative while the sedimentation rate ranged from 8 to 30 mm. In seven patients with full-term pregnancy with no complications, the test was weakly positive in two and negative in five and the sedimentation rate varied from 35 to 50 mm. Blood collected at autopsy from accidental death in four patients was also negative for CRP.

Of 42 patients with infectious hepatitis, 16 gave positive reactions. Of 26 patients with cirrhosis of the liver in whom secondary infection was ruled out 18 gave the reaction for CRP. In two patients with primary and one with secondary carcinoma of the liver blood collected at autopsy was found to be strongly positive for CRP. The patients with infectious hepatitis who gave positive tests for CRP were more severely ill and the case fatality rate in these patients was about 10 times higher than in those with negative tests. Similarly patients with cirrhosis who had positive tests were in worse condition than those with negative results. Biopsy specimens from these patients were suggestive of a smoldering necrosis, fibrosis, and mononuclear infiltration.

The electrophoretic pattern showed a greater fall in total plasma proteins in those with positive as compared to those with negative tests and also in albumin, alpha-1 globulin, beta globulin, and gamma globulin fractions, but the fall in alpha-2 and gamma globulin fractions was less. Other diseases besides liver diseases were also studied for CRP. Positive tests were observed in patients with rheumatic pericarditis, myeloid leukemia, multiple myeloma, Hodgkin's disease, rheumatoid arthritis, visceral leishmaniasis, and hemolytic anemia. The test was strongly positive in those with visceral leishmaniasis but became negative after treatment. Although the test for CRP has the same significance as the sedimentation rate, the author believed it to be superior as it is simpler and is more uniformly negative in normal subjects. This is especially helpful in normal pregnancy when the sedimentation rate goes up while the CRP test is negative or weakly positive. The test may serve as a valuable adjunct to liver function tests and to differentiate postnecrotic cirrhosis from cirrhosis following fatty change.

Ascorbic Acid Levels and Influenza.—P. S. Vaishwanar and co-workers *(Indian Journal of Medical Sciences,* vol. 13, July, 1959) believed the estimation of the ascorbic acid level in whole blood to be of greater significance than that of serum or plasma in assessing nutritional status as the plasma value represents only the immediate nutritive or metabolic level depending on the recent dietary intake. The authors studied the blood ascorbic acid level in 66 children, in 28 of whom the estimations were made first in March, 1957, and again in July, 1957, immediately after an influenza epidemic. In the other 38 only single estimations were made after the epidemic in August, 1957. The figures for blood ascorbic acid in children with no history of influenza were higher than those who had had the disease. The ratio in some was almost 2:1. In those for whom figures before the epidemic were available it was seen that the difference in the level in those with and without the history of influenza was the result, and not the cause, of infection. If the ascorbic acid level played any part in determining resistance to infection, it must have been small.

SPAIN

Protection Against Ionizing Radiations.—At the First National Medical Congress of the Spanish Red Cross held in Madrid in May the following conclusions were reached: It is necessary to inform the public about the dangers of radiologic pelvimetry and of serial intestinal roentgenography in pregnant women and to limit the amount of irradiation to all patients. All persons who work with ionizing radiations must be examined periodically, and temporarily removed from their tasks if their exposure to radiation exceeds the limits of safety. The public must be reassured that nuclear energy plants have developed complex systems of protection not only for the personnel working in those plants but also for the surrounding areas and that such plants do not represent a danger for the adjoining populated areas if the protective systems are adequate and properly operated.

Furthermore, the mobile installations of nuclear energy in submarines, and the portable army installations, or those in areas of difficult supply of usual fuel should not offer any danger to the waters where they navigate, the ports where they anchor, or the zones where they are stationed. The Red Cross should provide specialized teams and personnel to provide adequate care to any victims of accidents that might occur in isotope plants or laboratories. The Red Cross should also organize specialized aid units throughout the nation, in collaboration with civil defense personnel. All members of these units should be able to give first aid to victims of blast, thermal, and irradiation injuries caused by an atomic explosion.

Interauricular Septal Defects.—At the same meeting, Dr. Enrique Garcia Ortiz and co-workers presented a study of 40 patients with interauricular septal defects. They found that cyanosis is always associated with pulmonary arterial hypertension and with an increase in pulmonary resistance. It is rarely observed in young persons without circulatory decompensation, and it is always a consequence of massive arteriovenous shunt. In adults cyanosis appears in patients with cardiac insufficiency, complete arrhythmia, and an enlarged heart. Cardiac insufficiency is characteristic of interauricular septal defects. Sometimes an arteriovenous shunt persists and the arterial hypertension is inconstant. In this type of cardiopathy the elevation of pressures in the refilling of the left ventricle does not necessarily cause myocardial failure.

The radiologic changes in the pulmonary arterial tree continue to be a reliable sign of interauricular septal defects. The heart is enlarged, especially in the forms associated with great pulmonary deficit and marked arterial hypertension. The electrocardiographic changes reveal acquired abnormalities in which a complete bundle-branch block represents the last stage which may regress after the surgical closing of the septal defect. The hemodynamic examination shows, in most patients, a normal venous saturation. In more than half of the patients mixed shunts are observed. The curves of pressures obtained simultaneously in both auricles indicated that the mechanism of pressures at the auricular level was not sufficient to explain the direction of the shunts. In patients with an increase in the pulmonary deficit, pulmonary arterial hypertension is slight or moderate, but in those with an increase in arterial resistance it is severe.

The treatment consists of an open repair with use of hypothermia or prostigmin. This treatment should give satisfactory results in cases of patent foramen ovale, ostium secundum, and simple ostium primum, since the time limit is sufficient for closing these three types of septal defects. In a patient in whom there was drainage of the abnormal pulmonary veins, it was possible to divert the flow from the septum and to close the defect with complete success. The authors believe that, in patients with a common atrioventricular canal, hypothermia should not be applied but the heart-lung machine should be used.

SWEDEN

Hydrocortisone During Operation.—B. Aldman and co-workers (*Svenska läkartidningen*, June 26, 1959) gave hydrocortisone to patients during operation. They classified these patients as acute operative emergencies or elective cases. For the first category hydrocortisone was given by intravenous drip or injection in doses of 100 mg., a total of 100 to 300 mg. being given during the operation, and 100 mg. by intramuscular injection morning and evening for two days after the operation. A further 100 mg. was given by intravenous injection if a postoperative fall of the blood pressure threatened. For the elective cases 100 mg. was given by intramuscular injection for two days before operation or on the morning of the day of operation. During the operation 100 to 300 mg. was given by intravenous drip or injection. During each of the first postoperative days 100 mg. was given twice by intramuscular injection. This treatment did not interfere with the healing of wounds and it may have improved the operative prognosis, particularly for those threatened by flagging of the suprarenal system.

Tobacco Addiction.—In 1955 Dr. B. Ejrup (*Svenska läkartidningen*, July 3, 1959) started giving injections of lobelin hydrochloride to heavy smokers. By the end of 1957 he found that 93% of these patients got some benefit from the injections. Early in 1958 the first polyclinic for the weaning of heavy smokers was opened, and a little later there were six such clinics. In cooperation with various organizations combating tuberculosis and cancer, Ejrup sought to turn these clinics into research centers. He has had to rid the public of the notion that his treatment is based on a single drug, his ambition being to devise a system or series of simple measures suitable for general application to the control of the smoking habit. At the Danish equivalents of the Swedish polyclinics the patients pay for each drug injected, but in Sweden no separate charge is made for the drugs as it is desirable to feel free to vary the drugs or to give placebos for the sake of comparison. About 150 physicians cooperate with the polyclinics in compiling the observations made, and in Stockholm alone there are about 2,000 smokers whose reactions have been recorded. From his experience with the staffs of two industrial concerns, Ejrup estimated that Sweden, with a population of 7 million, has at least 150,000 nationals in need of his polyclinics. The commercial interests linked to the sale of tobacco need not, in his opinion, be alarmed about his polyclinics which are not waging war on tobacco in general, but only on the abuse of it by a small fraction of the population.

Corneal Opacities from Chloroquine.—According to Dr. O. Gabinus and co-workers (*Svenska läkartidningen*, July 10, 1959) since January, 1958, chloroquine has been given at the Jönköping General Hospital to patients with rheumatoid arthritis and other collagen diseases, the usual maintenance dosage being 250 mg. daily after twice to four times this amount in the first few weeks of treatment. Side-effects were on the whole negligible, but of the 19 patients examined with a corneal microscope 8 showed epithelial and subepithelial deposits on the lower half of the cornea. These diffuse opacities were homogeneous with the exception of those in one patient in whom they were slightly granular. No other abnormalities of the eyes were detected.

UNITED KINGDOM

Koilonychia.—Koilonychia is generally attributed to iron deficiency. Jalili and Al-Kassab (*Lancet* 2:108, 1959) investigated the incidence of this disease in patients with severe anemia, but they could find no correlation between the severity of the anemia and the occurrence of koilonychia. There was no statistical difference between the hemoglobin levels of patients with and without the condition. The nails were not deformed in some patients with a hemoglobin level of 1.5 to 3 Gm. per 100 ml. It was therefore concluded that iron deficiency alone does not explain the changes in the nails. In view of the poor protein intake of the patients and the fact that cystine is an important constituent of nails and is responsible for the crosslinkage in the polypeptide chains which contributes to the strength of the protein structure, cystine, arginine, and histidine levels in the fingernails of the patients were determined. The cystine in the nails of 29 normal subjects averaged 8.12%. It was independent of sex and social status. The cystine content of the nails of patients with koilonychia was much lower, averaging 2.54%. It was also low in patients with anemia without koilonychia, the average being 6.32%. The cystine content of the nails of two patients with koilonychia rose greatly and became more than double the initial value after increasing the protein content of the diet. The histidine and arginine content of the nails in koilonychia was within normal limits. According to Jalili and Al-Kassab a deficiency of sulfur-containing amino acids is a factor in the pathogenesis of koilonychia.

Hemoptysis due to Endometriosis.—Endometriosis is occasionally found in extra genital situations, such as the intestine, peritoneum, bladder and, rarely, the lung. Fleishman and Davidson describe the occurrence of hemoptysis in a woman, who at first was thought to be suffering from pulmonary tuberculosis, although a chest film, bronchoscopy, and bronchography did not reveal a tuberculous lesion (*Lancet* 2:88, 1959). When it was discovered that hemoptysis regularly coincided with the onset of menstruation a diagnosis of pulmonary endometriosis was made. The hemorrhage diminished, although it did not stop, when 25 mg. of testosterone dipropionate was given a few days before the expected period. When the hormone was stopped the hemorrhage from the lung was severe. Radiographs and tomograms taken between the menstrual periods were normal, but when taken the day before the expected date of menstruation a small area of infiltration was observed in the left upper lobe on two occasions. A lobectomy was planned but was not done as the hemoptysis diminished in severity and eventually stopped. Although histological proof was lacking it was believed that the lung lesion was endometriosis. The eventual cessation of hemoptysis despite continued normal menstruation and the inconstant radiologic appearances were attributed to the gradual sequestration of the ectopic endometrium via the draining bronchus.

MISCELLANY

MEDICINE AND AUTOMOBILE RACING

Frank E. Barnes, M.D., Smithfield, N. C.

Automobile racing has been known in the United States for years. From the old Vanderbilt Cup races on the Motor Parkway of Long Island, N. Y., in the early 1900's, racing has grown to a major sport. Before World War II crowds were drawn to Indianapolis, to hundreds of fairground dirt tracks, and to see the mighty midgets race on the 1/10-mile ovals throughout the many cities of our country. The daredevils of the 20's and 30's drove without restrictions or regard for personal safety. Death claimed many from their ranks in those days, from either faulty machinery, faulty road surfaces, or questionable driver qualifications. Medicine was seldom mentioned, in the heyday of dirt track racing.

Soon after World War II, small, racy, noisy sports cars began to make their appearance in the United States. The MG was the first to catch the fancy of sports-minded Americans. With the first invasion of foreign cars came a new sport—road racing. Europe had known road racing for years and European cars were built for this type of driving. Instead of in an enclosed oval, where speed was essential for winning, road racing took place on country lanes and city thoroughfares. This type of driving required more dexterity and stronger gear boxes than the ordinary oval track racing would ever require of a car. A road course might run from border to border of a country, such as in the Mexican Road Race, or follow a twisting, turning, dangerous course through a city, as in the yearly race at Monaco on the Mediterranean coast. The road races of Europe have been run on public roads closed to traffic on the day of the race.

The first attempts to establish road racing in the United States were at Watkins Glen in upstate New York and Bridgehampton, L. I. These races whetted the American appetite for fun and thrills and a new sport was born.

Problems quickly arose, however, and indignant townspeople forced the termination of racing on public roads. Racing quickly moved to airports, where spectator control could be enforced. Gen. Curtis Le May was instrumental in establishing many fine airport racecourses at Army air bases throughout the country. Disgruntled GI's and vote-happy congressmen soon put a stop to racing on government property, however, even though the proceeds from the races were filling the enlisted men's club treasuries. This handicap was in turn overcome by the establishment of privately owned, hard-surface racecourses across the country, from Limerock, Conn., down to Danville, Va., and out to Riverside, Calif.

Medical observers, some of whom are drivers themselves, became increasingly aware of the need for safety standards on American racecourses. Physicians began to investigate accidents. It soon became apparent that regulations governing racing would have to be enforced. Even though the driver considered it "sissy" or "uncomfortable," he would have to abide by the rules, if he wished to drive. The Sports Car Club of America (SCCA) became the governing organization for most amateur races in America. The directors and officers were men of foresight. Accidents caused public concern; death is certainly a cause for indignation. A medical advisory committee was established within the organization. This committee was given authority to enforce safety regulations at all Sports Car Club races.

The first directives were met with varied reactions, but the doctors were patient and soon noted compliance with all their regulations. As racing picked up in momentum, so did research. Dr. George G. Snively of California upset the manufacturers of helmets by condemning one helmet after another. With the aid of research departments at different universities, he could determine the resistance to stress of the materials used in making racing helmets. Helmets of drivers involved in accidents were also studied and defects noted. After many months of impartial investigation he made his recommendations, and they have become regulations for drivers on the SCCA racecourses today. Of course, manufacturers were indignant, but some were grateful and improved their products until they, too, were acceptable.

Along with the helmets went the problem of visors or goggles. Many types are on the market and there are as many adherents to each of the different designs. Recently the "blister" type of visor has been introduced and has been found satisfactory, if made of the right type of plastic and worn properly. The acetate and butyrate plastics are the best, since they do not shatter and will not leave jagged, pointed edges to cut facial tissues. The nitrates will give the same protection but are highly inflammable and thus are not used. These plastics are soft and scratch easily, compared to acrylic plastic, but this only necessitates care when they are not in use. Visors or goggles with metal supports are not recommended. The California Sports Car Club has outlawed all goggles not set in rubber. Any visual protection made of glass is also discouraged. Eyeglasses made of shatterproof plastic are now on the market, and they have been recommended for drivers who must wear glasses.

Most European drivers will not wear a safety belt. They feel they have less chance of getting hurt if they are thrown clear of the car instead of riding into a crash stop. American drivers feel they have

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Medical Director of Virginia International Raceway; member, Medical Staff, Grand Prix Races, Sebring, Fla.

less chance of injury if they remain within the car. This has caused much discussion, and no definite solution has been found; but the Sports Car Club of America insists on safety belts. They have based their regulations on research work done by scientists at Cornell University and on investigation of accidents. It has become a known fact that fewer Americans would have been killed in the past years if they had not been thrown from their cars during accidents. You are safer within the car. When a crash is followed by fire, the Europeans might be right; but the danger of fire is small compared to the possibility of getting crushed by a rolling car or a following car. Most medical men and automotive engineers agree that safety belts are imperative.

Safety devices can also cause injury, however. The width of the belt, where it is anchored to the car, and the type of buckle are all-important. A 3-in. width is recommended for racing and not less than a 2-in. width should be used in passenger cars. A thin belt could cause undue trauma to abdominal and pelvic organs after a severe impact. The belt should rest not across the thighs but at a 45-degree angle across the pelvic bone. The belt should be fastened to the frame of the car and not just to the seat, since the seat can easily tear loose and throw its occupant into the air on the first roll of the car. Even with a belt, men have had their faces injured by hitting the steering wheel. The shoulder harness would prevent this and would also prevent many whiplash injuries to the neck. It has recently been recommended by many safety experts that a shoulder harness plus a seat belt should be worn by drivers at all times. Buckles on belts can be annoying, especially when they lock and the driver cannot release the belt after an accident. The airline type of locking buckle is acceptable, but attempts are being made to improve this.

The roll bar has caused many a "he-man" to sneer, yet today one will not see a sports car, stock car, or any professional racing car without this simple protection. A bar of sufficient strength behind the driver's head, anchored to the car's frame, is lifesaving. Hard tops on cars can crush easily, and the roll bar is just as important to the hardtop car as it is to the convertible. Some American manufacturers are considering incorporating a roll bar into the windshield support of every car.

Fires are infrequent but a definite problem. Drivers are advised to wear flame-resistant coveralls which are fitted tight around the neck, wrist, and ankle. They should wear driving gloves to protect the hands and adequate shoes to protect the feet from harm. Clothing is easily rendered flame-resistant by immersion in a boric solution. Each automobile must have a fire extinguisher in the cockpit before it can be given approval to race.

Inspection of automobiles does not come under medical problems, but it has become an important part of racing. Before a practice run can be made on a course, each automobile is gone over by a qualified mechanic. If the brakes, lights, and condition of the tires are unsafe for fast-speed driving, the automobile is not permitted to run. This protects the driver as well as others on the course who might become involved in an accident caused by faulty equipment. Along with automobile inspection goes driver inspection. Before every endurance race a driver must submit to a physical examination. Heart, lungs, and eyes are all checked. One or two drivers are always weeded out by these examinations. As far as sprint racing is concerned, all SCCA drivers must receive a yearly physical examination. The background of the driver, with regard to epilepsy, insulin reaction, heart disease, fainting, and any disease that might influence reflexes, is investigated. The physical examination must be completed with care and attention to detail, including the eye examination.

Physicians have also become aware of the psychologically unfit driver. "That man will kill himself within a year," is a remark frequently heard at a racecourse. Since these drivers often do kill themselves, it is up to the physicians to try to weed out these drivers before they do harm to themselves or others. Some drivers flirt with death on every turn; other drivers have superior reflexes and can drive the car to the limit of its capacity. It is difficult to disqualify a man because he drives fast, but the medical recommendations are being accepted when most consultants believe a driver is psychologically unfit to race. A driver has an opportunity to appeal to a board of directors and can call his own physician in his defense. Physicians are doing their best to protect the majority from a reckless few. A psychological test is under study that may help to eliminate unfit racing drivers as well as unqualified Sunday drivers on our local highways.

Many believe the physicians interested in racing and sports-car activities are eccentric and are wasting precious time. Little publicity has been given the medical men working on improving highway safety through their racecourse laboratories. Dr. Snively's work on helmets has caused the California highway police to seek recommended head protection for their motorcycle force. Safety belts first used in racing have been advised for all passenger cars. Tires tested and punished at races are now on our everyday cars. Brakes, which were most inadequate for our heavy, high-powered passenger cars, have recently been improved by American manufacturers but only after much pressure from medical men and engineers who realized that power needs a halter. The work being done by the Cornell group and Dr. Miles O'Brien at Limerock, Conn., will soon influence every roadway constructed in America. Dr. O'Brien is conducting a series of tests for night driving and night blindness.

His report on these studies will be concerned with the effects of lighting and the causes of nighttime accidents.

The racecourse itself is not the physician's concern, but track officials are now seeking and listening to the medical directors who can foresee a dangerous situation. Doctors interested in trauma have developed insights into the causes of injury. Drivers and officials have finally realized that the course physicians are primarily interested in the health and safety of the drivers and not in speed records.

The American Association for Automotive Medicine was formed by a small group of physicians at the Sebring International Races three years ago. This group has grown to include over 40 members from coast to coast. The primary aim of the organization is to reduce accidents and injuries on racecourses. It is hoped that through their work with high-speed vehicles they will be able to persuade manufacturers and automotive engineers to improve safety features on our roads and in our family automobiles.

713 Hancock St.

MEDICAL FILM REVIEWS

Management of Burns, Part I: Supportive Care (PMF 5318); Management of Burns, Part II: Local Care (PMF 5319): 16 mm., color, sound, showing time: part I, 17 minutes; part II, 14 minutes. Produced in 1958 by the Department of the Army. Procurable on loan from the Surgeon of the Army Area in which the requestor resides or on purchase from United World Films Inc., 1445 Park Ave., New York 29.

Part 1 of this film covers the diagnosis, care, and treatment of patients suffering from burn injuries and points out that early supportive care is vital for recovery. Initial hospital procedures for treatment of burns are outlined, with stress on accurate appraisal of injury; sedation; establishment of a venous life line; requirement for tracheotomy; maintenance of patient's urinary output; planned fluid therapy; and use of hematocrit to determine relative amounts of plasma and corpuscles in the blood. The importance of building up the patient's morale for ultimate recovery is emphasized. In part 2, the essentials of supportive care are reviewed. Then, the steps of local care are presented, including cleansing of the wound; débridement of the skin; treatment with occlusive dressing; air treatment; and skin grafting. These are excellent films and the procedures used are those that are generally accepted as most satisfactory for this kind of injury. The films are highly recommended for physicians, medical students, and all hospital personnel who take part in the treatment of the burned patient, including nurses, hospital technicians, and aids. It would also be of value to people who have had advanced training in first aid and who may be involved in the care of mass casualties.

Help for Young Hearts: 16 mm., black and white, sound, showing time 14 minutes. Produced in 1958 by Potomac Film Producers for and procurable on loan from American Heart Association Film Library, 267 W. 25th St., New York 1.

The central theme of this film is that a child who has been held back by rheumatic heart disease can, with proper medical supervision and vocational guidance, grow up to normal living and become a useful member of the community. It emphasizes the part medical prophylaxis and vocational counseling can play in helping young people whose hearts have been damaged by rheumatic fever and also shows how parents are learning to protect children who have had rheumatic fever against recurrence of the disease. It points out that parents of the child with rheumatic fever may obtain information about protective drugs from their physicians or through local heart associations. A key point in this film is that it emphasizes what these children can do rather than what they cannot do and shows that the children can assume some responsibility of their own with regard to such matters as taking their medicine. This film is recommended especially for parent groups and for the training of professional people who will be working with children, such as physicians, social workers, teachers, nurses, physical therapists, and youth leaders.

Mouth to Mouth Resuscitation for Respiratory Emergencies: 16 mm., color, sound, showing time 18 minutes. Prepared in 1958 by and procurable on loan from Archer S. Gordon, M.D., 4614 Sunset Blvd., Los Angeles 27.

This film details the physiological requirements for effective artificial respiration and outlines the experimental and practical background of the development of mouth-to-mouth resuscitation. Regular and slow motion views depict the preferred techniques for mouth-to-mouth and mouth-to-nose resuscitation for children and adults. The use of an airway and mask are also demonstrated. The necessity for speed, maintenance of a clear airway, and adequate ventilation are emphasized. This film covers the subject of resuscitation without presenting large amounts of detail and in addition to the mouth-to-mouth method demonstrates three manipulative methods which have been effective. The photography is magnificent, the narration is clear, the action is efficient, and the film will be immediately intelligible and instructive to audiences of any age. It will appeal to physicians and is also recommended for showing to nonprofessional groups.

Total Hysterectomy: 16 mm., color, sound, showing time 27 minutes. Prepared by Somers H. Sturgis, M.D., Boston. Produced in 1958 by Sturgis Grant Productions, New York. Procurable on loan from Winthrop Laboratories, 1450 Broadway, New York.

The purpose of this film is to depict the author's technique for total hysterectomy in the manner in which it is taught to surgical residents at the Peter Bent Brigham Hospital. It follows the steps of the operation, including a preliminary dilatation and curettage, and contains diagrams to clarify surgical features as well as photomicrographs to document the case which is presented. In this film, the operation was performed on a 33-year-old mother of three children who was found to have a positive vaginal smear on a routine medical checkup. Cervical biopsy specimens showed carcinoma in situ. The patient first is operated on from below for a curettage and examination under anesthesia. Then she is placed, recumbent, into a modified Trendelenburg position, and total hysterectomy is performed through a transverse incision well superior to the pubic hairline. The color and photography of this film are excellent and it is recommended for physicians and medical students.

A Three-Stage Repair of Hypospadias: 16 mm., color, silent, showing time 13 minutes. Prepared in 1958 by and procurable on loan from S. Harris Johnson, III, M.D., and Matthew Marshall Jr., M.D., 509 Peoples E. E. Bldg., Pittsburgh 6.

This film demonstrates a three-stage operative technique for the repair of hypospadias. The method of repair, while based on techniques previously described, has been devised by the authors. There is reconstruction of the urethra from skin not only from the penis but also the scrotum. Construction of straight corpora cavernosa, a large-caliber urethra, and a meatus in a relatively normal position have been accomplished with a low incidence of relatively minor complications. The photography is excellent, and one can easily follow the operative procedure for this special technique. Since it is a very technical film and skips about rapidly, only urologists and plastic surgeons would be able to follow this technique intelligently, even with the captions that explain it. This film should be of special interest to urologists, plastic surgeons, and possibly some general surgeons who do certain types of plastic surgery. It is also recommended for residents in urology and plastic surgery.

Air Force Industrial Medicine in Action: 16 mm., color, sound, showing time 20 minutes. Produced in 1958 by the Department of the Air Force. Procurable on loan from Armed Forces Film Library Center, St. Louis 23.

This film illustrates the investigation and solution in an Air Force manufacturing establishment of an occupational health problem which attracted attention by an unusually high rate of absence due to illness in workers who performed a particular operation. It presents the philosophy that industrial medicine should be concerned primarily with prevention. While a more illustrative occupational health problem might have been selected, the film does show clearly the "team" approach necessary in occupational health, the plant physician, the industrial hygienist, the industrial nurse, and the supervisory personnel all being shown as contributing their particular skills to the solution of the problem. The photography is good, the production technique adequate, and the sound recording effective. This film is highly recommended for industrial physicians and others interested in industrial health.

The following films were produced in 1957 by and are procurable on long-term lease or purchase from Walt Disney Productions, 500 S. Buena Vista, Burbank, Calif. All are in color and sound and the showing time is 8 minutes each.

I'm No Fool as a Pedestrian: This film presents, through an animated cartoon with Jiminy Cricket as the moderator, the basic rules of safety for the pedestrian. The historical background of man from the stone ages up to modern times and the development of the automobile are portrayed. The film compares "you" as a safe individual and a "fool." It emphasizes alertness and the right and wrong safety measures to be taken by a pedestrian.

I'm No Fool Having Fun: The basic rules of safety and having fun are presented by Jiminy Cricket. The historical background presents the fact that, with the development of the machine and the 40-hour week, man began having more leisure time and, therefore, having fun. This film presents the basic rules of safety for such sports as hiking, swimming, skating, bicycling, and boating.

I'm No Fool in Water: The historical background of man and his use of water for recreational purposes is portrayed in the beginning of this film. It compares "you" as a safe individual and as a "fool" in the water. The film presents the right and wrong places for swimming and instills respect for water.

I'm No Fool with a Bicycle: This film shows the right and wrong ways of riding a bicycle and portrays the historical background of the bicycle. Jiminy Cricket conducts a contest between a "good boy" and an "ordinary fool"; the latter's disregard for safety leads to disaster.

I'm No Fool with Fire: This film illustrates the basic rules of safety with regard to fire as Jiminy Cricket points out the use and control of fire and the importance of fire prevention.

These are excellent films for children. They are logical in their presentation and very well organized. They will hold any child's interest and teach him the basic rules of safety in the situations shown.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Analysis of the Progress and Results Obtained in 134 Cases of Thyrotoxicosis with Radioactive Iodine (I^{131}). R. J. Soto, I. B. Rozados, O. J. Degrossi, F. A. Diez and others. Semana méd. 66:653-669 (May 21) 1959 (In Spanish) [Buenos Aires].

A group of 200 patients with hyperthyroidism was treated with I^{131}, which is at present the preferred iodine radioisotope for the treatment of thyrotoxicosis. This report covers the results obtained in 134 patients whose recovery or improvement was considered permanent. The majority of them (75%) were women, and the ages varied from 15 to 75 years, with the highest frequencies in the 40-55-year age bracket. Most patients were under 45. The group was classified into five subgroups according to the characteristics of the disease, namely, diffuse toxic goiter, nodular toxic goiter, thyrotoxicosis without goiter, cardiothyrotoxicosis, and recurrent thyrotoxicosis after surgical therapy.

The dose of radioisotope was established on the basis of the size of the thyroid (evaluated by palpation), and each patient received 200 microcuries per gram of the glandular weight, except for the group with recidivation. In the latter group the dose was 300 microcuries per gram. To avoid the induction of hypothyroidism, the maximal dose was kept at 20,000 microcuries for those with nodular goiter and at 15,000 for those with diffuse goiter. The median dose applied was 14,799 microcuries; the highest requirements were those of the patients with nodular goiter and with cardiothyrotoxicosis. The radioisotope was given orally while the subjects were fasting and after the blood cholesterol level, basal metabolism, and radioactive uptake had been checked. These tests were repeated every 2 or 3, 4 to 6, and 8 to 12 months after administration of I^{131}.

During the course of the treatment, 14 patients had temporary hypothyroidism with spontaneous recovery. Twenty-eight suffered slight loss of hair, and 16 developed a pain in the neck, with exacerbation of the thyrotoxicosis for a few days. Nineteen patients developed atrial fibrillation, which disappeared in 11 of of them. Permanent recovery was obtained in 127 patients; 5 became hypothyroid; and 2 abandoned the treatment. The time necessary for recovery varied between 3 and 4 months in the groups with diffuse, or without, goiter; the nodular forms required therapy for a longer period. The ophthalmic complication improved in 81 patients and became stationary in the others. These results were obtained with one dose of I^{131} in 98 patients, with 2 doses in 28, and with 3 doses in 5; only one patient required 4 doses.

Dietary Linoleic Acid and Linoleate: Effects in Diabetic and Nondiabetic Subjects With and Without Vascular Disease. L. W. Kinsell, G. D. Michaels, G. Walker and others. Diabetes 8:179-188 (May-June) 1959 [New York].

The authors discuss the relationship of dietary linoleic acid to a variety of plasma lipids in diabetic and nondiabetic subjects, many of whom had significant vascular disease. Some studies were carried out in ambulatory patients on semiconstant dietary intake, while others were carried out in patients on the metabolic ward receiving quantitatively constant dietary intake. The data presented in this paper appear to establish that linoleic acid administered either as purified ethyl ester or as naturally occurring fat, in sufficient quantity, in properly constructed diets, will reduce plasma lipids. Many vegetable fats lower levels of plasma cholesterol and other plasma lipids, but linoleic acid appears to be the constituent of these fats which is responsible for such effects. Generally speaking, the greater the amount of saturated fat in the diet, the greater the amount of linoleic acid required to produce a desirable lowering of plasma lipid levels. Because of major individual differences in response in patients with vascular pathology, lipidoses, etc., it is impossible to set up a ratio of relationships between dietary saturated and unsaturated fatty acids which will apply generally. In some diabetic and nondiabetic patients with vascular disease, subjective and objective improvement has been noted in association with the intake of diets containing large amounts of linoleate. It is still too early to state positively that such improvement is related directly to the diets employed. The fatty acid composition of the diet specifically influences the composition of the plasma cholesterol esters. High linoleate intake results in markedly increased plas-

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The place of publication of the periodical appears in brackets preceding each abstract.

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Influenzal Pituitary Depression. J. N. Mickerson. Lancet 1:1118-1121 (May 30) 1959 [London].

Debility, involving not only bodily discomfort but also impaired mental vitality, may persist in patients for many weeks after an attack of influenza. The author observed in 4 patients with influenza a similar pattern of symptoms, consisting of fatigue, muscular weakness, severe dyspnea, aching limbs, and mental depression associated with low blood pressure. These symptoms suggested adrenocortical insufficiency. Determination of serum electrolyte and urinary steroid excretion levels supported this view, but correction of hyponatremia and increased urinary steroid excretion after corticotropin administration indicated that adrenocortical insufficiency was secondary to reduced anterior-pituitary activity. Rapid improvement occurred in each patient during administration of corticotropin and later of prednisolone. In 1 patient severe mental depression and electroencephalographic abnormalities disappeared after steroid therapy.

Factors Influencing the Course and Prognosis of Systemic Lupus Erythematosus. R. P. McCombs and J. F. Patterson. New England J. Med. 260:1195-1204 (June 11) 1959 [Boston].

By analyzing the clinical data in 77 patients with systemic lupus erythematosus seen at the New England Center Hospital, Boston, the authors evaluated the prognostic implications of sex, age, manifestations of the disease, pregnancy complicating the disease, and corticosteroid therapy. While the disease occurred much less frequently in men, it was more severe and carried a much higher mortality than in women. When the diagnosis was established before the age of 21 years the prognosis was grave, but when the diagnosis was established after the age of 45 years it was favorable.

Evidence of renal involvement, even when the abnormalities of the urine were mild at first, was the most serious prognostic omen. Corticosteroid therapy did not prevent the progression of established renal disease, but it seemed to have some effect in preventing it, and certainly it did not induce it. Polyserositis and myocarditis, when not associated with renal failure, responded to corticosteroid therapy, and consequently prognosis in this group was favorable. Encephalitis, similarly, when not associated with renal disease, responded to corticosteroid therapy. Hemolytic anemia and thrombocytopenic purpura were occasional early manifestations of systemic lupus erythematosus but, in a small group, most patients who had these disorders later had serious features, from which many of them died. Pregnancy seemed to be a precipitating factor in the onset of some cases of systemic lupus erythematosus. However, once the disease was established, and in the absence of renal disease, pregnancy was safely undertaken with reasonable expectation of delivery of normal babies.

Corticosteroid therapy had a suppressive effect upon the rash, fever, pleurisy, pericarditis, peritonitis, pneumonitis, and hematological and neurological complications of systemic lupus erythematosus. It had little effect upon the renal lesions of the disease. Untreated patients usually died in the acute, "toxic" phase of the disease, whereas adequately treated patients had a much lower mortality. Deaths in treated cases were due to renal failure or complications of corticosteroid therapy.

The Management of Idiopathic Thrombocytopenic Purpura. A. A. Cooperberg. Canad. M. A. J. 80:937-943 (June 15) 1959 [Toronto].

Twenty-three consecutive patients with idiopathic thrombocytopenic purpura are reviewed in this paper. The disease is characterized by a hemorrhagic state associated with a reduction in the number of circulating blood platelets. Despite the low platelet count in the peripheral blood, the number of megakaryocytes in the bone marrow is normal or increased. Since Werlhof's first description of this disease, no effective therapy was available until 1916, when Kaznelson recommended splenectomy. There was no explanation for the success of splenectomy, and the operation is still performed on an empirical basis. All of the 23 patients had typical petechiae and other hemorrhagic phenomena, and platelet counts of less than 90,000 per cubic millimeter. Six were children under 6 years of age and 17 were adults over 19 years of age; 20 were females and 3 were males.

Cortisone, hydrocortisone, and prednisone were the corticosteroids used in the treatment of 14 of the 23 patients. The initial dose of cortisone was 200 mg. daily, of hydrocortisone 160 mg. daily, and of prednisone 40 mg. daily, in divided doses. The dosage was reduced as the platelet counts improved. Most patients were treated with prednisone. Three patients died of cerebral hemorrhage before corticosteroids were available. There were no deaths in those treated with corticosteroids. Of the 14 cases treated with steroids, 10 were acute and had a complete remission, whereas 4 were chronic with a temporary remission. Three of the patients with chronic purpura had a splenectomy which was followed by a complete remission.

It is concluded that all patients with thrombocytopenic purpura should be treated with large doses of corticosteroids as soon as the diagnosis is made. This applies to patients with thrombocytopenic purpura due to drug sensitivity and to symptomatic thrombocytopenic purpura as well. Hemorrhage is thus rapidly controlled and the platelet count is increased to normal. In most cases, splenectomy may be avoided. When thrombocytopenia recurs as the corticosteroid dosage is reduced, splenectomy will ultimately be required. Preparation of a patient for splenectomy with corticosteroids has made this a safe and elective procedure, rather than the hazardous emergency operation of former years. Where relapse occurs after splenectomy, the corticosteroids may be used either continuously or intermittently, as indicated, to reduce the risk of serious hemorrhage. To minimize side-reactions, small doses of steroids may be sufficient to attain the desired effect without attempting to reach normal platelet levels.

Macroglobulinemia of Waldenström and Gastric Ulcer. R. Cattan, P. Vesin, J. L. Bonnet and M. Hivet. Presse méd. 67:1068-1071 (May 27) 1959 (In French) [Paris].

Macroglobulinemia of Waldenström was demonstrated in a 63-year-old man admitted to the hospital because of 2 profuse hematemeses and subsequent melena complicating an ulcer of the lesser curvature of the stomach. The clinical, biological, and hematological aspects of the disease are described. The possible relation of macroglobulinemia of Waldenström to gastric ulcer, hepatic lesions, and the nosology of the disease was investigated, with particular attention to its connection with lymphoid leukemia, plasmocytic myeloma, and with certain forms of cirrhosis associated with hyperproteinemia.

Secondary Amyloidosis in Leprosy. Amyloidosis and Leprous Reaction. J. G. Masanti. Medicina 19:1-10 (Feb.) 1959 (In Spanish) [Buenos Aires].

Three hundred six patients with leprosy in the Baldomero Sommer Leprosarium of Buenos Aires were observed. The disease was lepromatous in 263 patients and benign in 43. The incidence and causal factors of amyloidosis were investigated. A diagnosis of amyloidosis was made by the clinical symptoms and by the results of either or both the Cohen and Benhold tests. The presence of amyloidosis was proved in 4 out of 160 patients with quiescent lepromatous leprosy, in 15 patients out of 100 with the reactional type of lepromatous leprosy, and in 2 out of 43 patients with benign clinical forms of leprosy. In all the patients with the reactional type of lepromatous leprosy the reactional bouts started within the first year from the appearance of leprosy. The reactions were severe, febrile, and recurrent. They were followed by the appearance of albuminuria (showing amyloidosic involvement of the kidney) within a period which varied between 7 months and 3 years after starting of the leprous reactions. The author concludes that lepromatous leprosy of the nonreactional type and benign leprosy are complicated by amyloidosis only in rare cases (2.5% and 4.5% respectively). Amyloidosis is frequent in the reactional type of lepromatous leprosy (15%). The main causal factor of amyloidosis is the acute reaction in itself. Amyloidosis of reactional leprosy rapidly damages the kidney, causing renal insufficiency and final uremia in a period of 1 to 5 years.

A Fatal Case of "Q" Fever Associated with Hepatic Necrosis. J. I. Tonge and E. H. Derrick. M. J. Australia 1:594-597 (May 2) 1959 [Sydney].

A meatworker, aged 52 years, had an acute attack of "Q" fever. Enlargement of the liver appeared on the 12th day, and jaundice on the 14th; death occurred on the 17th day. The patient's final illness was due, wholly or partly, to an acute infection with Coxiella burnetii. This diagnosis was established by the demonstration in mice of the characteristic Rickettsia organisms derived from the patient's urine, and by the development of specific agglutinins in his serum. Guinea pigs inoculated with urine and liver-kidney-spleen produced febrile reactions consistent with "Q" fever, and this effect was manifest in repeated passages. The lesions found at post mortem were widespread. The most prominent, and probably the most lethal, finding was the extensive, diffuse necrosis of the liver. Other findings were acute interstitial nephritis, interstitial pneumonia, bronchopneumonia, and encephalitis. The question whether the liver damage was due solely to C. burnetii or whether other factors contributed is difficult to answer on the evidence available. Hepatic involvement is often associated with an attack of "Q" fever, and the frequency of this association suggests a causal relation. It is also possible, however, that the patient had a simultaneous infection with the virus of infective hepatitis.

Studies of Erythrocyte Survival in Acute Leukemia. D. M. Whitelaw, K. A. Evelyn and P. F. Solvonuk. Canad. M. A. J. 80:944-948 (June 15) 1959 [Toronto].

The introduction of radioactive chromium for tagging red blood cells and estimating blood volume and erythrocyte survival time provided a relatively simple technique for evaluation of the presence and degree of hemolysis. The authors used this method in 12 patients with blast cell leukemias, in 10 of whom the disease first manifested itself as acute leukemia, one patient had polycythemia vera culminating in acute leukemia, and another one had chronic granulocytic leukemia, with an acute terminal phase. Most of the subjects were tested shortly after the diagnosis was made, but 1 patient was tested 4 months and again 8 months after diagnosis. In the method used, approximately 15 ml. of the patient's venous blood was withdrawn by syringe and injected into a sterile, silicone-treated, rubber-stoppered 100-ml. vial containing 5 ml. of acid citrate dextrose (ACD) solution and about 100 microcuries of Cr^{51} as $Na_2Cr^{51}O_4$ (radioactive sodium chromate). The mixture was allowed to stand at room temperature for 20 to 60 minutes, then 50 mg. of ascorbic acid was added in order to reduce the chromium remaining in the plasma to the trivalent form and thus prevent further uptake of chromium by the red blood cells. After thorough mixing, 10 ml. of chromated blood was drawn into a calibrated syringe and injected into the patient through the rubber tubing of a freely running intravenous infusion set. The remaining blood was used to determine the hematocrit value and to prepare samples of whole blood and plasma for radioactive counting at a later date.

It was found that the radioactive chromium method for studying red blood cell survival is applicable to short-term observations in acute leukemia where more prolonged studies would be impractical because of the necessities of treatment, including blood transfusions. It is essential that the red blood cell volume be measured at the beginning and at the end of the studies in order to correct the survival curve for alterations in red blood cell volume occurring during the experiment. About two-thirds of the patients studied showed a moderate or marked reduction in red blood cell survival. The curves showed a satisfactory degree of internal consistency and, where prolonged to 10 or 14 days, showed no tendency to deviate importantly from the early trend. While minor degrees of hemolysis might escape detection because of so brief a period of observation, it is evident that the method is sensitive enough to show hemolysis not brought out by other laboratory procedures. No correlation was apparent between the results of the survival studies and those of other laboratory tests used to indicate hemolysis. The rate of fall of hemoglobin value was closely related to the red blood cell survival.

Cryptococcosis: Further Observations and Experience with Amphotericin B. W. J. Martin, D. R. Nichols, H. J. Svien and J. A. Ulrich. A. M. A. Arch. Int. Med. 104:4-14 (July) 1959 [Chicago].

The authors studied 8 patients with cryptococcosis; the cases of 5 of these patients who had meningoencephalitis due to an infection by Cryptococcus neoformans, which was associated in 1 patient with Hodgkin's disease, are described. Cultures of the spinal fluid were positive for cryptococcosis in all 5 patients. Amphotericin B was administered by the intravenous route in 4 patients and by the intravenous, intrathecal, and intraventricular routes in the patient with Hodgkin's disease. The authors recommend that, when amphotericin B is given intravenously, each milligram of the agent should be dissolved in at least 5 ml. of 5% dextrose in distilled water. Treatment was started with an initial dose of 0.25 mg. of amphotericin B per kilogram of body weight, administered intravenously in 6 to 12 hours. The dose was gradually increased to approximately 1 mg. per kilogram of body weight, depending on the tolerance of the patient. Side-effects, such as phlebitis at the site of injection, headaches, flushing, chills, fever, dyspepsia, and azotemia, occurred; but these symptoms subsided when injections were administered at longer intervals, when the daily dosage was decreased, or when treatment was temporarily interrupted. The drug had no toxic effect on the hematopoietic system or on the liver function, and there was no evidence of irreversible damage to the kidneys.

The daily doses of amphotericin B, ranging from 50 to 100 mg. and administered for approximately 6 weeks, seemed to have arrested cryptococcic meningoencephalitis in 3 patients in whom the spinal fluid became free of fungi on repeated cultures. One patient was a treatment failure. Relapses occurred in 2 patients, one of whom had Hodgkin's disease, but even in the latter patient the drug afforded several months of continued existence. Final judgment as to the effectiveness of amphotericin B cannot be made, since the follow-up in these patients after termination of therapy has not been sufficiently long; however, it appears to be a promising anticryptococcic agent, even when the natural tendency of the disease to spontaneous remission of prolonged duration is taken into consideration.

The Syndrome of Acute Disseminated Moniliasis in Adults. A. I. Braude and J. A. Rock. A. M. A. Arch. Int. Med. 104:91-100 (July) 1959 [Chicago].

An attempt was made to define the clinical syndrome of systemic moniliasis and to determine the disturbance in resistance responsible for such infections in adults. The authors report a 55-year-old man with acute disseminated moniliasis and review 4 cases of this disease cited in the literature. The study has been limited to fatal cases of generalized moniliasis, in which the etiology was definitely established by isolation and identification of Candida albicans, and does not include localized infections of the meninges, lungs, or endocardium. There are 2 striking clinical features of this infection: (1) a background of continuous antibiotic treatment during a protracted debilitating illness, and (2) an abrupt decline in the clinical course with the development of fever, shock, mental depression, leukocytosis, and gastrointestinal hemorrhages. In 3 patients death occurred within 5 days after cultures revealed C. albicans. All the patients had been treated with one of the tetracyclines, and 3 had also received streptomycin and chloramphenicol. These antibiotics were given in large doses for periods ranging from 11 to 31 days before C. albicans was recovered by blood culture. Pancreatitis was the cause of admission in 2 of the patients, and neurological disease in another 2. The main findings at autopsy were mycotic abscesses of the kidney, heart, and brain. In 2 patients these abscesses were also found in the pancreas, and in 1 patient in the adrenal and the liver.

Culturally proved cases of the disease have been rarely recognized in adults, and no reports could be found in the literature before the advent of antibiotics. It is possible, therefore, that antibiotics play a decisive part in lowering the resistance of adults to C. albicans by suppressing the normal bacterial flora. Hypocalcemia, also a finding in the authors' patient, may have a possible significance in lowering host resistance to C. albicans. Nystatin has been effective in eliminating Candida organisms from the intestine and has an important place in prophylactic treatment of debilitated patients who are predisposed to moniliasis through prolonged antibiotic therapy.

Influence of Myocardial Infarction on Plasma-Lipoprotein Concentration. C. Dodds and G. L. Mills. Lancet 1:1160-1163 (June 6) 1959 [London].

Three methods of analysis—ultracentrifugation, Cohn fractionation, and paper electrophoresis—were used to study the lipoprotein patterns of the blood in a group of 220 healthy male volunteers, of an average age of 56 years, who had no clinical symptoms of coronary artery disease. The same 3 methods were used also in 2 groups of patients with coronary artery disease. The first group (group 1 infarcts) included 19 men who had suffered a myocardial infarct about 6 weeks earlier and from whom only one specimen was obtained. The second group (group 2 infarcts) comprised patients under treatment in hospital for myocardial infarction from whom samples were taken, where possible, within 24 hours of the attack, 3 or 4 days later, and thereafter at intervals of 7 days; this group included 78 patients of an average age of 58 years.

The measurements revealed that a myocardial infarction is itself associated with a pronounced lipoprotein abnormality which is manifest for at least 2 months after the attack. The condition of the lipoprotein pattern during this period cannot be summarized by a single measurement, and it is therefore inadmissible to compare analyses of this kind with those of a group of healthy men. The only certain way of separating the lipoprotein abnormalities due to an infarction from those which may precede it is to examine the blood of men both before and after an attack. The results obtained support the observation by others that the relatively acute atherogenic disease leading to myocardial infarction in young men (under 45) is preceded and accompanied by more pronounced lipoprotein abnormalities than the slowly developing coronary-artery disease of the elderly. In the latter, the lipoprotein patterns are more often "normal."

It may be concluded that the lipoproteins of the blood are, in certain cases, concerned with the development of coronary-artery disease and also that the effect of the infarct itself on the lipoprotein pattern has, in many cases mistakenly, been ignored. As a result, some investigators have used lipoprotein analyses with unwarranted confidence and freedom, while others have been undeservedly skeptical about them.

Acquired Hemolytic Anemia in Chronic Lymphocytic Leukemia and the Lymphomas: Survival and Response to Therapy in Twenty-Seven Cases. R. A. Kyle, J. M. Kiely and J. M. Stickney. A. M. A. Arch. Int. Med. 104:61-67 (July) 1959 [Chicago].

The records of 27 patients with hemolytic anemia associated with malignant disease, who were hospitalized at the Mayo Clinic between 1945 and 1957, are reviewed. Severe anemia was associated with chronic lymphocytic leukemia in 16 patients, with Hodgkin's disease in 7, with follicular lymphoma in 3, and with lymphosarcoma in 1. Hemolytic anemia was responsible for the initial symptoms and led to the diagnosis of the underlying disease in the majority of the patients with lymphoma, whereas in most of the patients with leukemia the diagnosis of anemia was made later. All the patients received standard treatment for their underlying malignant lymphocytic disease, including irradiation therapy, the administration of mechlorethamine hydrochloride and triethylene melamine, and blood transfusions. An attempt was made to evaluate the effect of adrenocortical steroids and corticotropin (ACTH) on anemia during 28 hemolytic episodes in 16 patients. The results of this therapy were exellent in 9 instances, fair in 15, and poor in 4. One patient who had received little benefit from cortisone responded dramatically to the intravenous administration of corticotropin. Also, another patient obtained complete remission by use of corticotropin, whereas he had had only temporary remission with cortisone therapy. There were only a few serious side-effects from adrenocortical medication because of the short duration of therapy in most patients. The response to cortisone and corticotropin therapy was not related to the type of underlying malignant lymphocytic disease. The effect of various standard treatments on the hemolytic process could not be individually evaluated.

The follow-up showed that among the 27 patients 8 were alive at the time of this report; 6 of these have had no particular trouble, either from the malignant lymphocytic disease or from the hemolytic process, and mild hemolysis has continued in 2. Eighteen patients died. The deaths of

8 were due to a combination of hemolysis and the malignant disease; 4 had no hemolysis at the time of death; no details about the deaths of the other 6 are known. One patient was lost for follow-up. It is important to recognize the presence of hemolytic anemia in patients with chronic lymphocytic leukemia or with malignant lymphoma in order to institute proper therapy. Although treatment with adrenocortical steroids and corticotropin has little to offer patients with chronic lymphocytic leukemia or with malignant lymphoma without the association of hemolytic anemia, these drugs often bring about remarkable improvement in patients with this complication.

Treatment of the Angina Syndrome: Results of the Use of Iproniazid. J. A. Barrera and R. G. Turiella. Prensa méd. argent. 47:111-115 (Jan. 9) 1959 (In Spanish) [Buenos Aires].

Fifty outpatients who had been given a diagnosis of angina pectoris (established by history and [illegible] evidence of ischemia, cardiac [illegible] infarction) were treated with iproniazid. There were 33 men and 17 women in the series, their ages ranging from 30 to 80 years. The patients received an initial dose of iproniazid of a lower level than usual, i. e., 75 mg. daily, divided into 3 doses of 25 mg. Only in the severer cases was the daily dose increased to 150 mg. The average duration of treatment was approximately 68 days. Each patient reported for examination once a week. The results of this therapy varied from complete relief from the symptoms of angina pectoris to no relief. According to the degree of relief reported, the patients were divided into 5 groups. The improvement obtained was estimated as 100% in group 1 (17 patients or 34% of the total series); 75% in group 2 (8 patients or 16% of the total number); 50% in group 3 (14 patients or 28% of the series); 25% in group 4 (5 patients or 10% of the series); and 0 in group 5 (6 patients or 12% of the series). The beneficial effects of iproniazid were manifest within one week to one month of the therapy. In some patients the improvement persisted even after discontinuation of the treatment; in others the symptoms reappeared on omission of the drug and again disappeared when the treatment was reinstituted. Thirty-two patients suffered side-effects of varied kinds and degrees. Six of them experienced sexual impotence, which in one persisted even after the administration of iproniazid had been suspended. The intensity of the undesirable effects led to the interruption of the treatment in 15 patients; in 5 of these it could be reinstated.

It is the authors' impression that the administration of iproniazid is the first effective therapy encountered in treating the angina syndrome. They point out the danger of untoward effects, however, and recommend the use of smaller doses than usual, especially at the start. The initial dose should be 75 mg. or less, and the patients should be closely watched during the entire treatment.

Prednisone Given Alone and in Combination with Chloramphenicol in the Treatment of Typhoid: Clinical, Bacteriological, and Serologic Observations in 100 Cases. C. F. Colucci. Presse méd. 67:725-728 (April 11) 1959 (In French) [Paris].

Clinical studies have been carried out to evaluate the effect of synthetic glucocorticoids, given alone or in conjunction with chloramphenicol, in a total of 100 patients with mild typhoid. All the patients presented practically identical initial agglutinin levels; the duration of their disease ranged from 10 to 20 days, and no treatment had previously been given them other than symptomatic therapy. The patients were divided into 3 groups. The first group consisted of 36 patients who were given prednisone orally, or prednisolone by injections, for periods ranging from 10 to 18 days, in total doses varying from 550 to 870 mg., depending on body weight. The second group of 34 patients received prednisone orally, or prednisolone parenterally, for a period of 12 days, with total doses of 215 to 310 mg., depending on body weight; these patients were also simultaneously given small doses of chloramphenicol for 14 days, the total dose varying from 14 to 18 Gm., depending on body weight. The third group consisted of 30 patients who served as controls and who were given small doses of chloramphenicol alone for 18 days, with total doses ranging from 18 to 23 Gm., depending on body weight. Symptomatic treatment was also given to all the patients.

Comparison of the results obtained in the 3 groups showed that cortisone and the synthetic glucocorticoids are well tolerated even if administered for a prolonged time, but that their therapeutic action is limited when given alone. These drugs have proved to be significantly inferior to chloramphenicol. The best results were obtained in the second group with the administration of chloramphenicol in conjunction with prednisone or prednisolone, which brought about a rapid cure, without recurrence, in 50% of the patients. The results obtained with chloramphenicol in association with prednisone or prednisolone were far superior to those obtained with either these hormones or chloramphenicol alone.

The author advocates administering synthetic glucocorticoids in association with chloramphenicol in small doses for fairly long periods, with total doses ranging from 215 to 310 mg. for glucocorticoids, and from 14 to 18 Gm. for chloramphenicol. This regimen produces, in addition to a reduction of the excessive organic reaction, a gradual bacteriostasis with the help of the immunizing powers of the body. Thus, the damage that may be caused by bacteriolysis can be avoided, because, on the one hand, this is produced gradually, and, on the other, the body is protected against it by the prolonged hormone therapy.

Factor-VII Deficiency with Christmas Disease in One Family. F. Nour-Eldin and J. F. Wilkinson. Lancet 1:1173-1176 (June 6) 1959 [London].

The incidence of Christmas disease or plasma thromboplastin component deficiency is estimated at about 2 per million of the population in England and Wales. Congenital deficiency of factor VII seems to be even rarer. The authors present 2 related patients (a 21-year-old man and his 76-year-old maternal grandfather) whose clinical picture and family history suggested a hemophilia-like disease. Routine blood-clotting tests showed, in both cases, a combined deficiency of factor VII and Christmas factor. A study on the effect of the plasma of these patients on the stage of plasma thromboplastin formation demonstrated the presence of Bridge anticoagulant, thus proving the presence of true Christmas disease. It is shown that the conjoint anomaly was inherited as a sex-linked recessive character.

Coarctation of the Aorta Followed for Twenty-Five Years. H. Cookson. Lancet 1:1178-1180 (June 6) 1959 [London].

A diagnosis of coarctation of the aorta was made in 1933 in a 38-year-old woman. She had angina of effort, anxiety symptoms, and a toxic goiter which was treated by total thyroidectomy in 1935; this operation had a good effect on all the symptoms. After 1936 she was not seen for 6 years when she reported that over this period she had been "wonderful" and had been able to do her own housework, but she now had pain in the region of the left breast and in the left arm, throbbing in the neck and ears, some falling-out of her hair, and a feeling of cold. Moreover, the skin was dry and coarse, and there was slight cardiac enlargement, coarse duplication of the apical first sound, and a late-systolic murmur. There was further gradual deterioration during the next 15 years; the electrocardiogram of 1933 and the one taken on the day of death in 1958 were very similar, although transient ischemic T-wave changes had been recorded in the intervening period. During this time the brachial blood pressure showed some variations, but there was little change in the mean pressure throughout the course, the systolic reading falling and, to a less extent, the diastolic reading rising. In spite of the burden of hypertension, which was probably life long, and the severe and extensive coronary obstruction, heart failure of an incapacitating degree did not occur until 4 days before death. The almost exact similarity of the final electrocardiogram to the one taken 25 years previously, despite the finding of extreme coronary narrowing, is to be explained by the equal distribution of the ischemia throughout the myocardium, with no local area of acute necrosis.

The review of Reifenstein and associates in 1947 put congestive heart failure as the third commonest cause of death in patients with coarctation, excluding incidental causes, which head the list. Rupture of the aorta and bacterial endocarditis or aortitis were found to cause death more frequently than congestive failure. In the case reported by the author, massive calcification of the aorta proximal to the coarctation may have protected it from rupture, while the normal aortic cusps would lessen the liability to endocarditis.

Edematous Malignant Exophthalmos Revealing a Leukosis: Pathogenetic Discussion. H. Giroire, A. Charbonnel, J.-P. Kernéis and P. Lemouroux. Presse méd. 67:817-820 (April 22) 1959 (In French) [Paris].

The authors present the case of an 18-year-old youth with malignant edematous exophthalmos that was the first sign of a leukosis. On admission to the hospital, the patient said that the exophthalmos had appeared suddenly while he was in good health 2 months before the observation. Weakness, pallor, and some loss of weight were noticed at this time. Ophthalmological examination revealed that the exophthalmos, measured with Hertel's exophthalmometer, amounted to 26 mm. in each eye. Visual acuity was perfect, the fundus oculi was normal, and the field of vision was complete. Basal metabolism was increased slightly, but the iodine fixation test gave normal results. The blood test, which was the key to the etiological problem, showed a red blood cell count of 2,650,000 per cubic millimeter and a white blood cell count of 18,400, while the percentage of leukoblasts was 95%. The patient was given Cortancyl with transfusions, and later Purinethol and antibiotics; then he had 5 sessions of radiotherapy to the retro-orbital region. Thereafter the general condition of the patient improved, the body weight increased, the red blood cell count increased to 5.5 million per cubic millimeter, while the white blood cell count dropped to 11,000, and the leukoblast percentage to 90%. The condition of the eyes improved greatly: the edematous infiltration of the eyelids became less marked, the exophthalmos was reduced to 23 mm. in each eye, and complete closure of both eyes again became possible. The retinal vessels became more accentuated, and the retina looked striated, especially in the interpapillary ocular region. A mild edematous infiltration near the temporal segment of the papilla, with no hemorrhage or exudate, was noticed on the left side, however. This aspect of the fundus oculi revealed the incipient edematous infiltration of the retina.

Sometime later the patient returned to the hospital with severe stomatitis, greatly enlarged cervical lymph nodes on the left side, and fever. The red blood cell count had decreased to 2 million per cubic millimeter, while the white blood cell count had increased to 29,000, and the percentage of leukoblasts to 100%. The condition of the patient became increasingly worse. Rapidly generalized purpura set in, followed by profuse visceral hemorrhage, progressive coma, and death. On autopsy, the pituitary origin of the exophthalmos was confirmed. The authors point out that the hypophysis may secrete an exophthalmos-inducing hormone differing from the so-called thyrotropic hormone and that leukosis should, therefore, be considered as one of the conditions that may cause edematous malignant exophthalmos by way of a hypophysial infiltrate.

Aludrine Test and Peripheral Leukocytes. F. F. C. Moreno. Rev. clin. españ. 72:151-155 (Feb. 15) 1959 (In Spanish) [Madrid].

When establishing the diagnosis of a pulmonary condition, it is of great importance to determine whether the cause is a functional reversible process or an organic irreversible change. The Aludrine test is recommended by the author as adequate for this purpose. Eighteen patients, taken at random as they applied for consultation, were given the Aludrine test after a preliminary determination of total pulmonary capacity, quantity of air expired, velocity of expiration, and leukocytic formula. Aludrine was administered in a 1/1,000 solution and inhaled in 12 deep inspirations. The test was considered positive when on repetition of the determinations made before the inhalation of Aludrine there was an increase in the respiratory output, especially in the velocity of the expiration and in the volume of air expired during the first second after a deep inspiration.

Of the 18 patients studied, 11 showed positive results and 7 negative results. In the group with a positive test, 8 patients showed also an increase in the number of peripheral leukocytes, 1 showed negligible increase or decrease, and 2 showed a definite decrease. In the negative test group, there was only one patient with a definite increase in peripheral leukocytes, while 5 had negligible variations and one had a definite decrease. A comparison of the leukocytic formulas, taken before and after the test, indicated that variations in the number of leukocytes were produced mainly at the expense of the granulocytes, especially of the eosinophils. The author concludes that the implication of a positive Aludrine test is the existence of a reversible bronchial spasm, which is improved by medication, and that the accompanying leukocytosis constitutes the response to another pulmonary function, i. e., the regulation of peripheral leukocytes.

Treatment of Crohn's Disease with Deltacortisone. R. Crismer and C. Drèze. Acta gastro-enterol. belg. 22:229-243 (April) 1959 (In French) [Brussels].

Deltacortisone (or prednisone) was used in the treatment of 8 patients with Crohn's disease (distal, regional, or terminal ileitis). The first 2 patients showed a temporary improvement, not, perhaps, entirely due to the drug, which lasted for 3 months. Deltacortisone, however, did not prevent the development of intraparietal fistulas in these 2 patients or the extension of the disease process in one of them. It should be noted that in each case the disease had reached a stage in which fibrosis secondary to edematous reaction was such that deltacortisone was incapable of preventing the complications of lymphatic blockage. The results, in general, seem to show that deltacortisone is effective in the treatment of Crohn's disease when it is still in the follicular stage of ileitis, either primary or recurring after operation. The disappearance of pain and diarrhea in such cases is usually accompanied by the restoration of anatomic and radiologic integrity.

The benefit derived from deltacortisone seems to be due, on the one hand, to its effect on the general condition and, on the other, to its anti-inflammatory and antifibroblastic effect. Its action is probably potentiated by the concomitant administration of antibiotics. The authors prescribed deltacortisone in a daily dose of 20 mg., sometimes for several months, combined with sulfaguanidine (8 Gm.) and chloramphenicol (2 Gm.) to prevent the infectious complications sometimes associated with the use of deltacortisone, and to assure good intestinal sterilization. Deltacortisone was well tolerated by all the patients, although glossitis appeared in one in whom a laryngeal smear revealed the presence of Candida albicans.

SURGERY

Considerations of the Rationale and Technique of Coronary Endarterectomy for Angina Pectoris. J. A. Cannon, W. P. Longmire Jr. and A. A. Kattus. Surgery 46:197-211 (July) 1959 [St. Louis].

In the course of experience with the direct surgery of obliterative atherosclerosis of the terminal aorta and its distal branches, it occurred to the authors that the pathological manifestations in the coronary arteries are comparable to those found in the femoropopliteal region of the arterial tree. Obliterative atherosclerosis is a disease of relatively large vessels. Its obstructive component tends to be maximum in the region of arterial bifurcations. The primary disease is the subintimal collection of lipoprotein which results in narrowing and eventual occlusion of the lumen. Thrombus formation is encountered only as a secondary phenomenon. In the treatment of femoropopliteal obliterative disease, one of the authors developed a semiclosed technique of endarterectomy, based upon the fact that a definite cleavage plane exists in atherosclerosis between a relatively intact outer arterial wall consisting of media and adventitia and the thickened subintimal plaque. It is also to be noted that the occlusions are segmental, and the arterial tree distal to an occlusion tends to remain patent. The continued patency of this distal tree is the essential requirement for successful direct arterial surgery.

After using the semiclosed thromboendarterectomy successfully in the treatment of the popliteal and posterior tibial arteries, it occurred to the authors that the same technique with suitable modification might be applicable to obliterative coronary atherosclerosis. Since that time a research program has been under way to study the possibility. Investigation of this problem has been pursued along 4 main avenues: (1) pathological study of coronary atherosclerosis in terms of feasibility of direct surgical attack; (2) elaboration of a surgical technique; (3) determination of criteria for candidate selection; and (4) clinical experience. Pathological findings justify coronary endarterectomy in severe angina pectoris due to obliterative coronary atherosclerosis. The feasibility of reestablishment of blood flow through a formerly obstructed coronary arterial segment has been proved by animal experimentation. An objective method permitting diagnosis, case selection, and postoperative objective evaluation of results has been elaborated. The authors show in illustrations the special instruments used and also the basic steps in the technique of coronary endarterectomy by intraluminal stripping under direct vision.

Nine patients with severe intractable angina pectoris were subjected to coronary endarterectomy. Five survived the operation, and all have shown improvement as measured by subjective and objective clinical evaluation and as confirmed by postoperative treadmill exercise electrocardiograms. The greatest problem in accomplishing the operation did not so much concern the dissection on or in the arteries, or problems of removing the proximal or distal core, or problems in closure of an arteriotomy. Rather, it concerned the intermittent myocardial sluggishness and irritability especially of the left ventricle.

Thyroid Cancer and Its Treatment. J. W. Welch, C. A. Hellwig, V. E. Chesky and E. N. McCusker. Surg. Gynec. & Obst. 109:27-37 (July) 1959 [Chicago].

At the Hertzler Clinic, Halstead, Kan., 3,024 patients were operated on for thyroid disease in the 15-year period from 1940 to 1956. Pathological studies confirmed the presence of thyroid cancer in 267 (or 8.8%) of these. The authors divide the thyroid carcinomas into 2 groups, a favorable and an unfavorable one. The favorable group includes pure papilloma, papilloma with follicular variant, follicular carcinoma, Hürthle cell carcinoma, invasive adenoma, and clear cell carcinoma. In this favorable group the over-all survival rate was 80%. The unfavorable group includes giant cell carcinoma, small round cell carcinoma, malignant lymphoma, hemangio-endothelioma, and diffuse carcinoma. In this unfavorable group the over-all survival rate was 35%.

The authors believe that conservative surgery alone, consisting largely of lobectomy and bilateral subtotal thyroidectomy, is adequate therapy for the less malignant forms of thyroid cancer. In the more malignant forms therapy should consist of total thyroidectomy, with a modified neck dissection and postoperative adjuvant therapy. The authors agree with Crile as regards the fallacy of the radical en bloc dissection for thyroid cancer. They show that excision of all involved lymph drainage and involved contiguous structures cleanly and en bloc is incompatible with life. A modified neck dissection (excision of all involved nodes which can be dissected free) is more pragmatic. This type of surgery may then be followed by hormone therapy, in the form of desiccated thyroid extract.

Surgical Treatment of Achalasia of the Esophagus. C. Edward, B. Abbot, W. C. MacKenzie and C. A. Ross. Canad. J. Surg. 2:345-352 (July) 1959 [Toronto].

Twenty-five patients with achalasia of the esophagus, who have been operated on, form the basis of this review. Twenty-two patients were treated by a modified Heller operation, while 3 had various reconstructive procedures on the gastroesophageal junction. Heller used an esophagogastric extramucosal myotomy anteriorly and posteriorly. The abdominal approach is favored by most surgeons for patients with achalasia of the esophagus. In the 22 patients undergoing the modified operation, the authors used the abdominal approach 12 times and the thoracic approach 10 times. With the abdominal approach for the modified Heller operation, a midline incision is used, and the left lobe of the liver is mobilized well to the right by dividing the left triangular hepatic ligament. The peritoneum over the esophagogastric junction is divided transversely and the esophagus mobilized from its bed by blunt dissection with a finger. The left vagus nerve is identified and retracted to the right. The incision should extend far enough distally to be sure that all esophageal fibers are divided, and it should be kept to the right of the midline. The length of this incision will average 8-12 cm., and the mucous membrane should bulge freely into view. When the procedure is complete, there should be no evidence that any circular bands of muscle fibers are constricting the mucosa. No attempt is made to approximate the peritoneum over the defect in the muscle wall.

Seventeen of the 22 patients in whom the modified Heller operation has been used obtained excellent results with no recurrence of dysphagia and no clinical evidence of regurgitation or esophagitis. Two patients have been classified as having had a good result, although an occasional bout of dysphagia has been experienced, especially when eating too rapidly. In 3 patients a poor result was obtained; however, review of the records revealed that insufficient indications were present to warrant the operative procedure. All 25 patients have been assessed, and no case has been lost to follow-up. Two patients have died of causes other than achalasia of the esophagus. In the group treated by a modified Heller procedure, the follow-up period averaged 3 years and 2 months. In the small group treated by gastroesophageal reconstruction, the time since operation has averaged 11 years. The authors conclude that a modified Heller esophagocardiomyotomy is the treatment of choice in achalasia of the esophagus.

Metabolic and Physiologic Observations on Patients Undergoing Extracorporeal Circulation in Conjunction with Hypothermia. W. G. Young Jr., W. C. Sealy, I. W. Brown Jr. and others. Surgery 46:175-184 (July) 1959 [St. Louis].

Since January, 1956, intracardiac surgery has been performed on 111 patients at the Duke University Medical Center in Durham, N. C., utilizing a combination of extracorporeal circulation at moderately low flow rates and hypothermia. The authors present an analysis of the metabolic and physiological changes occurring in these patients during and after perfusion at an esophageal temperature of 28 to 32 C (82.4 to 89.6 F). For details of the extracorporeal circuit including heat exchanger, DeWall-type bubble oxygenator, and Sigmamotor pump, the authors refer to an earlier report. The induction and control of hypothermia were greatly improved by the incorporation of an efficient blood heat exchanger in the last 73 of the 111 patients.

It was found that at flow rates averaging 54 ml. per kilogram per minute for individuals under 35 kg. (78 lb.) in weight, and 31 ml. per kilogram per minute for heavier individuals, venous oxygen saturation can be maintained within the normal range if the esophageal temperature is reduced to 28 to 32 C (82.4 to 89.6 F). At this flow rate and temperature, metabolic acidosis is not encountered to a degree greater than that seen accompanying any major surgical procedure. Postoperative metabolic acidosis does not occur if myocardial efficiency is adequate. Oxygen consumption in patients perfused at 28 to 32 C was found to approximate one-half of that occurring at 37 C (98.6 F). Successful correction of severe tetralogy of Fallot in a patient whose esophageal temperature was reduced to 9.3 C (49 F) is described. Profound hypothermia permitted the use of very low flow rates, allowed temporary cessation of perfusion, and obviated the need for cardioplegic agents.

Implantation of Yttrium 90 into the Pituitary Body of Five Patients with Acromegaly. A. M. Dogliotti, A. Ruffo and G. M. Molinatti. Minerva med. 50:1575-1578 (May 23) 1959 (In Italian) [Turin, Italy].

This study concerns 5 patients with acromegaly, who were treated by implantation of 5 small rods of radioyttrium (Y^{90}) through the nostril into the pituitary body. Three patients were followed up for a period of over a year, and 2 for 4½ months and 45 days, respectively, after the operation. The therapy produced subsidence of headache, sweating, excessive thirst, and backache; improvement in asthenia and polyphagia; and diminution in swelling of the extremities, tongue, and face. Less benefit was obtained for disorders of sexual function, except that libido was restored in one patient. Amelioration of the subjective symptoms was marked during the first month of therapy, but was less intense afterwards.

Phosphatemia, which had been present in one patient, was restored to normal values 22 months after the operation. Normalization of carbohydrate metabolism was obtained in 2 patients. A decrease of basal glycemia and of daily glycosuria was observed in one patient 13 months after the implantation. A slight disorder of carbohydrate metabolism, which was present in one patient before the implantation, deteriorated 45 days after the operation. This condition, however, may improve and may eventually disappear, because a similar change took place in 2 other patients whose carbohydrate metabolism normalized after the third postoperative month. Calcium metabolism was restored to normal 3 months after implantation in those patients who had a negative calcium tolerance test before the operation. Intense polyuria, which had developed immediately after the implantation, subsided within 15 to 20 days. No diminished function of the thyroid, adrenals, and gonads was observed.

PEDIATRICS

Intrahepatic Biliary Atresia. L. J. Krovetz. Journal-Lancet 79:228-235 (June) 1959 [Minneapolis].

Detailed histories are given of 2 patients with intrahepatic biliary atresia, who were seen in recent years at the University of Minnesota Hospitals in Minneapolis. One of these patients is still alive at 16 years of age and is in good health except for severe generalized pruritus. This represents the longest period of survival of a patient with this condition that has been reported to date. The literature on both extrahepatic and intrahepatic biliary atresia is briefly reviewed. Only 23 cases of intrahepatic biliary atresia have been reported. Nine of these patients have survived more than 3 years, 6 of them being still alive when reported. The median age of survival of infants with extrahepatic biliary atresia which has not been relieved by surgery is only 4 to 6 months.

Dermatomyositis in Childhood: Report of Studies on 7 Cases and a Review of Literature. J. W. Carlisle and R. A. Good. Journal-Lancet 79:266-273 (June) 1959 [Minneapolis].

The histories of, and observations on, 7 children (4 girls and 3 boys) with dermatomyositis, who were studied at the University of Minnesota Hospitals, Minneapolis, since 1954, are presented. Age at onset ranged from 6 months to 13 years. Family histories failed to reveal other members with dermatomyositis, scleroderma, or acute lupus erythematosus. Insidious onset was characteristic. However, within weeks, the entire spectrum of skin manifestations, with the classical eyelid and butterfly heliotrope rash and extensor surface erythema, was evident. Periorbital edema was observed in all cases. Edema of ankles and hands was frequently present. Two children showed the chronic skin changes, described as poikiloderma, and consisting of atrophy and increased pigmentation of the skin. Calcinosis was observed by roentgenologic examination and biopsy in 3 cases. Palatorespiratory involvement with severe intercostal muscle weakness and late cardiac failure developed in one child, and death ensued. Fever was not a prominent feature in this series. Several children showed exacerbation following mild respiratory infection. In one child, the rash became more severe after exposure to sunlight. Dermatomyositis could not be related to bacterial or viral infections. Electrophoretic patterns were obtained on 6 of the children. Elevation of the alpha-2 globulin and gamma globulin components was regularly revealed. Examination of skin and muscle biopsy specimens by light microscopy demonstrated nonspecific myositis. The diagnosis must depend on the clinical manifestations.

The question of therapy remains unsettled. Three of the 7 children treated with steroids showed continued progression of weakness, pain, fever, and rash throughout steroid therapy. On the other hand, 4 children had a less severe course during moderate steroid therapy. However, 3 of these children showed calcinosis by x-ray examination. With the exception of specific change on biopsy or improvement on specific muscle testing, it is most difficult to relate prognosis to steroid therapy. The absence of dramatic improvement in response to steroid therapy and the high incidence of gastric or duodenal ulcers (3 of 6 children) raise the question of whether or not steroid hormones should be used in these patients.

Pulmonary Congestion and Edema as a Complication of Acute Nephritis in Childhood. R. A. Toro-Nazario and E. C. Burke. Journal-Lancet 79:246-253 (June) 1959 [Minneapolis].

Pulmonary edema is an uncommon, though serious, complication of glomerulonephritis in children. Because the authors could not find a report of the incidence of this complication in pediatric patients with nephritis, they examined the records of all children with acute or chronic glomerulonephritis seen at the Mayo Clinic in the years 1950-1957 to ascertain the frequency and clinical course of this complication. In this 8-year period, 89 cases of acute nephritis and 4 cases of chronic nephritis were encountered. A table listing the various complications of nephritis in these 93 children shows that 5 had pulmonary edema. After reviewing the literature on the subject, the authors discuss the clinical aspects, pointing out that pulmonary congestion and edema as a complication of nephritis can be acute and fulminating, with all the signs and symptoms of cardiorespiratory embarrassment, or it can be insidious, producing few, if any, clinical findings. Pulmonary edema may be transient and may subside rapidly as the general condition of the patient improves, or it may lead rapidly to death. The fact that the edema can be subacute, with few clinical findings, may explain, in part, why this condition is so rarely recognized.

Roentgenographically, pulmonary congestion and edema of the lungs appear as symmetrical, irregular, and diffuse areas of increased density located centrally or basally. The changes occur as a result of the intra-alveolar edema and congestion and dilatation of the pulmonary blood vessels. Either of these processes may predominate. If the change is primarily due to intra-alveolar edema, the affected regions may appear nodular, simulating metastatic or inflammatory pulmonary lesions. If vascular congestion and dilatation predominate, a picture of generalized hypervascularization, not unlike that seen in uncomplicated left ventricular cardiac decompensation, is present. This condition must be differentiated roentgenographically from such widely dissimilar diseases as sarcoidosis, chronic miliary tuberculosis, cystic fibrosis of the pancreas, parenchymal inflammatory diseases, and neoplastic infiltration.

The histories of 3 patients in whom pulmonary congestion and edema complicated acute glomerulonephritis are presented. Hypervolemia is the main etiological factor in this complication in nephritis, and varying degrees of left ventricular failure rarely contribute to the final picture. The authors emphasize that this complication can remain clinically silent and that it should be suspected and looked for in every case of nephritis, even in the absence of evidence of congestive heart failure. Return of renal function effects diuresis and clearing of the pulmonary edema. Fluid allowances must be kept minimal, covering only insensible losses plus urinary output during the period of oliguria.

Prognosis of Fetuses at 33 Weeks' Gestation in Rh-Sensitized Women Who Have Had Preceding Stillbirths. G. Biering, I. Kaiser and W. Krivit. Journal-Lancet 79:277-283 (June) 1959 [Minneapolis].

The prognosis for the fetuses of women who are Rh-sensitized and who have had a preceding stillbirth is known to be poor. Delivery at or before 35 weeks of gestation is one of the methods advocated as a means of reducing the mortality rate. Early termination of the contact with maternal antibodies has been considered as a method of preventing the erythroblastosis from progressing to severe hydrops and subsequent death in utero. The results obtained by early delivery have been difficult to analyze because of lack of true control series. This paper presents a retrospective study of the prognosis of fetuses alive at 33 weeks' gestation in Rh-sensitized women who had had preceding stillbirths. From 1945 to 1957, 119 liveborn infants and 21 fetal deaths in utero were recorded at the University of Minnesota Hospitals in Minneapolis. In the mothers of 12 of the 119 liveborn infants and in 13 of the 21 fetal deaths in utero, a history of prior stillbirths was obtained. Eleven of these 25 pregnancies resulted in a dead fetus in utero before the 33rd week. Among the remaining 14 fetuses, who were alive at the 33rd week, there were 2 stillbirths, 1 hydropic infant, and 2 neonatal deaths due to kernicterus; thus, the final survival rate was 9 of 14, or 64%. The present series and review of the literature indicate great variability of the effects of isoimmunization. It is suggested that controlled clinical studies are necessary if convincing evidence of the value of early interruption of pregnancy is to be obtained.

Novobiocin in the Treatment of Bacterial Bronchopneumonia in Nursing Infants. L. Francalancia. Riv. clin. pediat. 63:248-258 (March) 1959 (In Italian) [Florence, Italy].

A group of 81 hospitalized nurslings with bacterial bronchopneumonia, aged up to 14 months, received a therapy of novobiocin, supplemented with penicillin, streptomycin, and chloramphenicol. The bacteriological examination of the material obtained from the pharynxes of the patients revealed the presence of the following strains of bacteria: Staphylococcus pyogenes var. aureus alone in 15 infants or associated with Streptococcus, Diplococcus, and Blastomyces organisms in 14; Staph. pyogenes var. albus in 2; gram-positive Diplococcus organisms in 25; streptococci in 8, gram-positive coccobacilli in 5; and other pathogenic agents in 8. Cultures of Staph. pyogenes var. aureus, isolated from the material obtained for testing, were sensitive to novobiocin and to erythromycin, but they were scarcely, or not at all, responsive to other antibiotics.

Daily dosage of novobiocin varied from 200 mg., divided into 2 oral doses, or 100 mg., divided into 2 doses administered intravenously, up to 500 mg., divided into 3 oral doses, or 200 mg., divided into 2 doses administered intravenously. The therapy with novobiocin produced remission of bronchopneumonia in 75 patients (92.5%) and deterioration of the clinical picture in 6. Remission of bronchopneumonia on roentgenologic examination was obtained between 5 and 12 days after the therapy with novobiocin began. This study suggests further use of novobiocin, combined with other antibiotics, for the treatment of bacterial bronchopneumonia in nursing infants.

UROLOGY

Use of Isoniazid Para-aminosalicylate for the Treatment of Genitourinary Tuberculosis. J. Cibert and J. Barbier. Presse méd. 67:841-842 (April 25) 1959 (In French) [Paris].

Isoniazid para-aminosalicylate, known also as pasiniazide, was used for 2 years in the treatment of 44 patients with genitourinary tuberculosis at the urologic clinic of Lyons, France. Fourteen of the cases were genital tuberculosis, and 30 were renal tuberculosis. In the genital tuberculosis group, 11 patients had a rapid clinical cure after being treated for 3 months, the diagnosis having been verified in 3 cases by epididymectomy. The 30 patients with renal tuberculosis were divided into 2 groups: one group had been treated for a long time with other medication and then were given pasiniazide; the other group received pasiniazide combined with streptomycin. Four of the patients with renal tuberculosis were seen in an advanced stage; they had intense cystitis, massive pyuria, and gross morphologic and functional changes on urography. The disease of 11 patients with renal tuberculosis was less severe; they had unilateral limited lesions, integrally conserved renal function, and only moderate morphologic changes. Ten of these patients were cured, but the condition of one, a 65-year-old man, was aggravated despite 4 months of treatment with 120 Gm. of streptomycin. Cystitis persisted after nephrectomy in this patient, and only after 3 months of postoperative treatment with streptomycin and pasiniazide was it cured.

Results of treatment with pasiniazide are comparable, if not superior, to those with other antituberculous agents. In the patients with renal tuberculosis, cure was regularly and rapidly obtained by using the combination of streptomycin and pasiniazide; later the cure remained stable with pasiniazide alone. In the patients with genital tuberculosis, good results that were rapid and sure were obtained with pasiniazide alone in the majority of cases. Failures were usually in those forms of genitourinary tuberculosis in which the antituberculous agents were generally ineffectual. In 4 cases, however, pasiniazide was well tolerated when aminosalicylic acid and isoniazid were not. Pasiniazide alone was generally used only in cases of genital tuberculosis, although 4 cured cases of renal tuberculosis in which it was used alone are cited. There were only 3 cases of digestive intolerance to the drug, and urinary tolerance was excellent. Nephritic colic appeared only in 2 patients who were receiving the combination of streptomycin and pasiniazide, but on withdrawal of streptomycin and continuation with pasiniazide alone the colic was cured.

OPHTHALMOLOGY

The Syndrome of the Aortic Arch: Ocular Manifestations of "Pulseless Disease" and a Report of a Surgically Treated Case. R. L. Tour and W. Fletcher Hoyt. Am. J. Ophth. 47:35-48 (May) 1959 [Chicago].

Takayasu in 1908 first adequately described the ocular manifestations of what was later to be called the "aortic arch syndrome." In spite of the fact that the associated eye findings represent only one facet of a far more widespread pathological state, the entire disease complex has in recent years been referred to as "Takayasu's disease." The ophthalmological aspects of this syndrome are due to hypoxia of ocular tissue. Hypoxia is also manifest in other organs, such as the brain, which are dependent for their nourishment on the patency of the large vessels arising from the aortic arch. Occlusion of these vessels, whether partial or total, results in a relatively characteristic disease, its severity depending upon the degree of such obstruction. The authors list 12 different terms under which the syndrome has been described. They discuss its signs and symptoms and review the pertinent literature. They believe that the term "aortic arch syndrome" should be applied to this condition.

The visual symptomatology results from the greatly altered blood supply to the head. Since both common carotid arteries are occluded in the aortic arch syndrome, these patients experience transient loss of vision in one or both eyes. The retinal blood supply may be sufficiently low so that postural hypotension, resulting from a change from the reclining to the sitting position, will cause observable pulsation in the central retinal artery and segmentation of the blood column. Numerous other changes in the ocular structures occur as a direct result of chronic hypoxia. Early in the disease the fundus may appear normal, or there may be merely a few microaneurysms in the periphery of the retina. Dilatation of the veins with bead-like swellings are next noted, and finally arteriovenous communications appear which encircle the optic disk. Similar arteriovenous anastomoses are described in the conjunctiva, and attention has been called to the appearance of newly formed vessels running circumferentially at the root of the iris. The reduced blood flow to the ciliary body is also undoubtedly responsible for the greatly lowered intraocular pressure which commonly occurs as part of the syndrome. Late complications, occurring when the disease is well established, consist of cataract formation, optic atrophy, retinal detachment, retinitis proliferans, vitreous hemorrhage, and corneal opacification.

Syphilitic aortitis with or without aneurysm has been most commonly suspected as etiological in the aortic arch syndrome, but a nonspecific type of arteritis has also been suggested as a causal factor. The treatment should be directed toward the primary process. Antisyphilitic therapy is indicated if the serologic tests are positive, but little improvement can be expected after the great vessels of the aortic arch have become obstructed. It is hoped that the advances in vascular surgery will soon permit the radical reconstruction of the aortic arch. In this connection the authors present the case of a 50-year-old woman, who was successfully treated by surgical removal of obstructions in the major branches of the aortic arch. After the operation, ophthalmodynamometry provided dramatic evidence of the increase in retinal arterial pressure at a time when the carotid pulses could not be palpated because of neck dressings. The almost immediate rise of intraocular pressure from very low preoperative levels to almost normal was further evidence of the improved circulation to the head. The advances in cardiovascular surgery have greatly improved the prognosis of the aortic arch syndrome.

THERAPEUTICS

Observations on the Treatment of Pulmonary Tuberculosis with Sulfoniazid. M. Lucchesi. Minerva med. 50:1426-1433 (May 12) 1959 (In Italian) [Turin, Italy].

Sulfoniazid had a beneficial effect on 36 patients, some of whom were psychiatric patients, with active pulmonary tuberculosis. The drug, combined with 60 Gm. per day of an aminovitaminic sirup, was given for from 4 to 6 months in a daily dose of from 50 to 70 mg. per kilogram of body weight, divided into 3 equal subdoses. Some of the patients were given 50 Gm. per day of streptomycin, which was injected twice a day at the beginning of the treatment, every other day during the second month, and then every 3 days during the third month of treatment. Patients with severe lesions were also given a prednisone preparation. Laboratory tests made at the beginning, during, and after the treatment showed no changes in the composition of the blood or in the liver and kidney functions. The values of the erythrocyte sedimentation rate were high in most of the patients during the first 3 or 4 weeks of the treatment; afterwards they declined slowly and became normal or close to normal.

Sulfoniazid was tolerated well by all the patients. The results, especially when a large dose was given, were better than those usually obtained with isoniazid. Sputum became negative in 26 patients, some of whom had derived no benefit from previous prolonged treatment with other drugs, including isoniazid. Sulfoniazid, like other antituberculous drugs, in some patients had a marked beneficial effect on the general and pulmonary conditions, but had no effect on the sputum. The author believes that this may be due to adaptation of the bacteria to the antibacterial agent and to the selection of resistant individuals in a sensitive population, as well as to the progressive loss of virulence of the resistant strains. That the drug did not come into an efficient contact with the bacteria is a less probable hypothesis.

The author believes that the beneficial effect of sulfoniazid is connected with its bacteriolytic and bacteriostatic effects; the organism is freed in a rapid and progressive manner from the direct and indirect (biological and dynamic) harmful effect of Koch's baccilli and of their toxins. The possibility of giving the patient large quantities of the drug several times a day and for long periods of time makes sulfoniazid a useful drug in the treatment of the tuberculous psychiatric patient or of any other tuberculous patient from whom it is hard to obtain collaboration.

Treatment of Diabetes with N-N-Dimethyl Diguanide (LA 6023). E. Azerad and J. Lubetzki. Presse méd. 67:765-767 (April 18) 1959 (In French) [Paris].

N-N-dimethyl diguanide (LA 6023) was administered orally to 88 hospitalized patients with diabetes mellitus, aged between 16 and 75 years. The initial daily dosage consisted of 2 or 3 Gm. of the drug, administered as 3 or 4 tablets. Subsequently the dosage was decreased from 1.5 Gm. down to 0.5 Gm. a day. The results were good in 34 patients, fair in 35, and poor in 19. Younger patients responded better to the treatment than older ones. Obese patients with a mild variety of the disease benefited more from the treatment than did patients with a severe variety of the disease and with a tendency toward acidosis. Approximately one-half of the patients were receiving insulin treatment when the N-N-dimethyl diguanide treatment was instituted. It was possible to reduce, but not to eliminate entirely, the dosage of insulin in about two-thirds of the patients who received the combined treatment of insulin and N-N-dimethyl diguanide. The efficacy of N-N-dimethyl diguanide was weaker, the longer had been the preceding therapy with insulin. No severe side-effects to N-N-dimethyl diguanide developed. Moderate digestive disturbances, consisting mainly of nausea and diarrhea, were observed. Diarrhea induced discontinuation of the therapy in 4 patients.

PATHOLOGY

The Cytological Diagnosis of Solid Tumours by Small Needle Aspiration and Its Influence on Cancer Clinic Practice. I. H. Smith, J. H. Fisher, J. S. Lott and D. H. Thomson. Canad. M. A. J. 80:855-861 (June 1) 1959 [Toronto].

For some 20 years the Ontario Cancer Foundation's London Clinic, in conjunction with the department of pathology of the University of Western Ontario, has been studying the value of tumor aspirates as interpreted histologically from cut sections. A supplementary smear from the same material was occasionally made. At times from necessity when tissue fluid alone was obtained, or when the tumor proved to be cystic, the smear technique was used by itself. Gradually, and in particular since 1954, the curiosity of the authors has been replaced by the realization that the cytological interpretation of tumor aspirates has established itself as a most valuable procedure—surpassing and replacing the study of the sectioned aspirate in some instances and equalling it in others. Reliance is now placed on cytology to the extent that, when an aspiration is performed on an accessible lump, emphasis is placed first on obtaining tissue fluid for cytology, the plug forming a very important but secondary component of the procedure when and if procured.

The aspiration set consists of a 50-cc. Luer-Lok syringe, 20-gauge and 22-gauge needles of various lengths, and freshly prepared slides coated with egg albumin. The overlying skin is sterilized. If the no. 22 needle is routinely used, no local anesthetic is required. The tumor is immobilized with the left hand, and the needle is inserted until the tumor or its capsule is engaged. Maximum suction is employed, and the needle is guided through the tumor in 2 or 3 directions. When withdrawn, the tissue fluid within the needle is expressed on to the albuminized slides, 2 preparations being made. The material is smeared evenly by using the needle and, while the smear is still moist, the slides are immersed in fixative in a Coplin jar. Should a plug or excess tissue be available, it is placed in fixative for histological section. The smear is fixed for 15 minutes to one hour in fluid containing 1% glacial acetic acid in 95% ethyl alcohol. After fixation, and while still wet, it is stained with hematoxylin and eosin; it is then mounted and ready for microscopic examination.

The accuracy and clinical value of aspiration cytology has been appraised in 203 cases of cancer and 194 cases of deep-seated benign disease. A total of 524 smears was made. Exfoliative cytology and the cytology of effusions are not included in this study. In breast cancer 93% were confirmed cytologically, although in 18% more than one aspiration was required. Establishing diagnosis by this method permits a planned therapeutic approach and eliminates the need for frozen section examination in most instances. In lymph nodes secondarily involved by malignant disease, 94% of diagnoses were confirmed by aspiration cytology. There were 5 false-positive results (2.5%) in 194 benign cases; if interpreted in the light of clinical impression, this need be of little consequence. Of 203 malignant cases, 18 (8.8%) gave a false-negative result. Eight of the 18 were in breast lesions and required further histological investigation.

The simplicity, accuracy, and practical value of aspiration smear cytology for the solid tumor are established. The method deserves wider application. Although smear diagnosis of primary lymph node cancer is possible, it is still advisable to make the diagnosis histologically. No attempt was made to evaluate the accuracy of cytological smear examinations in benign diseases of the breast, but the authors feel that the psychological effect of establishing the diagnosis of cystic disease at once is most rewarding.

Hematomorphologic Determination of Sex: Determination of Sex from the Blood Picture. J. M. Caliezi. Schweiz. med. Wchnschr. 89:499-503 (May 9) 1959 (In German) [Basel, Switzerland].

All cytological methods of determining sex are based on a morphologic peculiarity of the cellular nucleus in females. The hematomorphologic method, the only one the author is concerned with in this paper, takes a special position in so far as the sex characteristic—a chromatin attachment of the cellular nucleus—differs greatly from that of the other body cells, in form as well as in percentage of occurrence and, moreover, numerous secondary forms of nuclear attachments may cause confusion. The author points out that Davidson and Smith, the discoverers of hematological sex differentiation, demanded that in order to identify a person as "female" it should be possible to detect among 500 mature neutrophil leukocytes 6 specifically female nuclear attachments, which they designated as "drumsticks." The absence of drumsticks was evidence that the individual was "male," that is, the diagnosis was made by exclusion. In this connection the present author asks, "What about the blood smears that show 5 or less drumsticks?"

Other investigators found that the typically female nuclear attachment is found in men on rare occasions, whereas still others denied this, pointing out that these attachments were only similar to, but not identical with, drumsticks. Although on the basis of his own observations the author accepts this last view, he points out that differentiation of these atypical forms from the female nuclear drumstick attachment is very difficult and in some cases impossible. He describes and illustrates drumsticks, clubs, bulbs (or sessile nodules) and also mentions pseudodrumsticks or small clubs, tags, and minor lobes. He established the percentage incidence of the various nuclear attachments in 65 females and 35 males.

He regards as definitely "female" a blood smear containing 3 specifically female nuclear appendages in 500 mature neutrophils. Drumsticks and clubs are specifically female nuclear attachments, and sessile nodules and the scanty occurrence of tags are indications of female sex. A blood smear containing no specific female nuclear appendages in 300 mature neutrophil leukocytes definitely can be considered as indicative of the male sex, and the frequent occurrence of tags and the absence of sessile nodules are indications of the male sex.

PUBLIC HEALTH

Tuberculosis in Medical Students at the University of Maryland. J. R. Karns. Am. Rev. Tuberc. 79:746-755 (June) 1959 [New York].

A tuberculosis control program was carried out on 2,302 medical students at the University of Maryland School of Medicine from 1934 to 1957. Only those who were observed for at least 1 year were included in this study. The survey showed that clinically significant tuberculosis had developed in 17 students while in school. The most striking feature was that in 16 of these the disease was diagnosed in the period from 1934 to 1950, whereas only 1 case occurred after 1950, indicating that the risk of tuberculous infection in the medical school has diminished in recent years. The reduction in morbidity has occurred without the use of BCG vaccine; it was brought about by early diagnosis, by spontaneous and improved treatment of tuberculosis as a contagious disease. Vollmer's test was positive in all students with clinically proved tuberculosis at the time of diagnosis. In a group of 53 students the patch test was found to be as accurate as the first-strength purified protein derivative (PPD). Since medical students are more exposed to the risk of tuberculous infection than any other student group, continuous vigilance is, therefore, necessary.

BOOK REVIEWS

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Physiology of Cardiac Surgery: Hypothermia, Extracorporeal Circulation and Extracorporeal Cooling. By Frank Gollan, M.D., Assistant Director of Professional Services for Research, Veterans Administration Hospital, Nashville. Beaumont Lecture, Wayne County Medical Society. Cloth. $4.50. Pp. 96, with 18 illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

This monograph, a brief survey of some new techniques applied in cardiac surgery, is focused primarily on selected basic physiological and biochemical problems; it also discusses some current controversies and possible areas for future investigation. The presentation, in general, is somewhat cursory, but there is an extensive and interesting section dealing with the role of combined extracorporeal cooling and circulation techniques in cardiac surgery. The style is highly personal and flavored with many quotations from Coleridge, Einstein, Shakespeare, and others. This monograph has a useful bibliography. It is valuable as an interpretative essay which discusses present problems and applications in this field from a historical perspective.

Abnormal Haemoglobins: A Symposium Organized by the Council for International Organizations of Medical Sciences, Established under the Joint Auspices of UNESCO and WHO. Edited by J. H. P. Jonxis and J. F. Delafresnaye. Cloth. $9.50. Pp. 427, with illustrations. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The symposium here reported took place in Istanbul under the auspices of a group of 50 international voluntary associations of specialists belonging to all the medical disciplines. The 26 papers, by different authors, with discussions, cover genetic and physical factors in the heterogeneity of hemoglobins, their identification and interpretation, clinical aspects, the hemoglobins in children and in different diseases, and the geographical distribution of different hemoglobins. Two papers deal with paper electrophoresis and serologic differentiation. An extensive bibliography is given, as well as a helpful index. The material is highly technical and presupposes a thorough knowledge of genetics, with an understanding of the exact meaning and true significance of such words as "genes," "alleles," "dimerization," "phanerosis," and "a propositus for the sibship." One should also have a working knowledge of electrophoretic, chromatographic, and salting-out techniques to understand the many figures in the text. The book contains a tremendous amount of data and should be extremely valuable to those working in the field of hemoglobins.

Current Problems in Allergy and Immunology. Papers dedicated to Béla Schick on occasion of his 80th birthday. Edited by William Kaufman. Cloth. $14.40; 60 Swiss francs. Pp. 992, with illustrations. S. Karger AG., Arnold Böcklinstrasse 25, Basel, Switzerland; Swiss Bank Corporation, New York, 1959.

This volume is composed of the articles published in four volumes of *International Archives of Allergy and Applied Immunology*. There are many excellent contributions in this book by masters of their subjects, mainly in the form of summations of material already published. Among the outstanding contributions are the papers on a comparison of fluorescein and radioactive iodine (I^{131}) as labels for antibodies, on the nature of tumor antigen, on the fate of labeled foreign antigens, on the immunological basis of carcinogenesis, on passive cutaneous anaphylaxis, on immunohematological disorders, on drug reactions, on the pathology of allergy, and on serologic reactions in rheumatoid arthritis. There are other good papers but, since there are more than 60 altogether, they cannot all be discussed or mentioned. Unfortunately, the good contributions are diluted by a number of mediocre or even poor and faddish expositions. This is the great weakness of the book and especially disturbing since such articles are given a stamp of respectability and authority when placed side by side with the works of truly great scientists. This is apt to mislead the uninformed reader. This volume, therefore, can be recommended only to those who already possess a good, discriminative acquaintance with the field.

Services to Blind Children in New York State. By William M. Cruickshank and Matthew J. Trippe. Syracuse University special education and rehabilitation monograph series 4. William M. Cruickshank, editor. [Brewster House book.] Cloth. $5. Pp. 495, with illustrations. Syracuse University Press, University Station, Box 87, Syracuse 10, New York, 1959.

This volume presents the results of a major study by the Syracuse University Research Institute. The stimulus for the study was the increased number of children blinded, particularly from retrolental fibroplasia. In New York state in 1956, there were 2,286 such persons under 21 years of age, and there was a probable total of 30,200 blind children in the United States. The principal objectives of the study were to determine the educational, social, and

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

health characteristics of the blind children in the state of New York, to determine the services available and used, to determine the nature of the programs offered by specialized and nonspecialized agencies for blind children, to study legislation, and to indicate areas of service to blind children.

It comes as a surprise to learn how inadequate the statistics are concerning blindness. In New York state only 33% of the children for whom annual visual appraisal was indicated had been examined within the year. This seems to be a particularly serious omission in the instance of 565 children with a diagnosis of "presumed blindness," of whom only 84 had been evaluated visually during the previous 12 months. The many physicians participating in local school board activities should find the following statement relevant: "The education of blind children with sighted children involves more, however, than a mere administrative decision. Blind children, wherever they are educated, must have programs equal to and exceeding those provided to sighted children. The public school administrator who decides to integrate blind children in the system must understand the implications of his decision in terms of personnel, equipment, orientation of general educators and other factors vital and essential to a satisfactory program." The importance of this statement is emphasized by the data which suggest that the residential school provides a more satisfactory education than the local school. The educational advantages of the residential school, however, must be weighed with other evidence which indicates that a more satisfactory emotional development occurs in the home environment.

The recommendations of this study for meeting the challenge of the blind child are, no doubt, applicable in a number of other states. The physician whose work brings him into contact with the blind should be particularly interested in this study of New York state and particularly with comparing the facilities offered by his own state.

Air Pollution Control. By W. L. Faith, Managing Director, Air Pollution Foundation, San Marino, California. Cloth. $8.50. Pp. 259, with illustrations. John Wiley & Sons, Inc., 440 Fourth Ave., New York 16; Chapman & Hall, Ltd., 37-39 Essex St., Strand, London, W. C. 2, England, 1959.

This book was prepared to provide the nonspecialist with a better understanding of the nature and problem of air pollution and present basic facts that must be considered in air pollution control programs. The introductory chapter defines air pollution and contains brief summaries of its effects on health, property, and vegetation. The author then discusses the effects of meteorological conditions on the distribution of air contaminants and the application of meteorology to air pollution control. The bulk of the subject matter is concerned with the technical, chemical, and engineering aspects of control under the following classifications: dusts, fumes, and mists; gases; and odors and automobile exhausts. In these sections there is information on chemical composition and physical properties of contaminants, sources of contamination, sampling and analysis techniques, equipment, and abatement methods.

Concluding chapters discuss the planning and requirements of air pollution surveys and legal aspects in the control of air pollution. An extensive bibliography is provided at the end of each chapter and there are numerous diagrams, tables, graphs, and photographs throughout the book. The author has made an authoritative, concise, easily understood presentation of an exceedingly complex subject. This text should be an excellent nontechnical reference source for basic information about the important aspects of air pollution.

Hereditary Transient Paralysis with Special Reference to the Metabolism of Potassium: Familial Periodic Paralysis, Familial Episodic Adynamia. By Uffe Sagild. [Thesis, M.D., University of Copenhagen.] Paper. Pp. 242, with illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1959.

Recent work on electrolyte balance has focused attention on potassium, the element which is of central interest in the present book. Of the two types of muscular weakness he describes, one can be induced by giving potassium chloride. The other, when it occurs, is remedied by the same drug. The value of this book lies mainly in the numerous chemical determinations of the potassium content of the blood and urine and in the application of tracer techniques (by means of radioactive potassium [K^{42}]) to determine the amount of exchangeable potassium and the rate of exchange between injected K^{42} and body potassium. In addition there has been an extensive investigation of the genetic background of the author's patients, so that in one instance it was discovered that two apparently distinct pedigrees were linked more than 200 years ago. Patients temporarily paralyzed by hypopotassemia have been falsely accused of malingering. Others, knowing their family history, have occasionally induced attacks for the purpose of malingering. To his own collection of cases of transient paralysis from Denmark and Sweden the author adds the information available from the more than 700 cases reported in the literature, and the book closes with a good bibliography and an index.

It seems desirable to comment on the unhappy choice of terms to designate the two conditions studied and on the state of medical logic as here illustrated. The differential diagnosis between "familial episodic adynamia" and "familial periodic paralysis" is given in tabular form on page 134. The critical reader cannot help but observe that if a spell of moderate muscular weakness lasting a few hours were to occur at any time of the day in a boy at the age of 10 years, even a study of his reflexes, his electromyogram, his electrical excitability, and the distribution of paralysis might not suffice to decide which condition he has and whether the administration of potassium on the basis of history and physical findings alone would prove lifesaving or fatal. The author asserts, on page 133, that the sole similarity between the two "diseases" is that both are "characterized by transient attacks of muscular weakness." His tabulation does not bear this out. The ultimate criteria are the chemical determinations of serum potassium and the patient's responses to administration of dextrose or potassium.

The conscientious student, likewise, must be confused by the words "episodic" and "periodic," which are used as antonyms. In reality neither of the conditions is periodic in the sense of recurring at regular intervals, and certainly there is nothing periodic about a single attack occurring in a man at the age of 70 years (page 188). The student will be further confused by the apparent distinction between paralysis and adynamia, which is hardly justified either by usage or by etymology. The habit of assigning arbitrary and unpredictable meanings to words and of implying distinctions where none are justified has long been an obstacle to clear thinking in medicine. It is to be hoped that a rational terminology for these two syndromes will be developed soon.

Atlas of Roentgenographic Measurement. By Lee B. Lusted, M.D., Associate Professor of Radiology, University of Rochester School of Medicine and Dentistry, Rochester, New York, and Theodore E. Keats, M.D., Professor of Radiology, University of Missouri School of Medicine, Columbia. Cloth. $9. Pp. 176, with 119 illustrations. Year Book Publishers, Inc., 200 E. Illinois St., Chicago 11, 1959.

For years busily practicing radiologists have surrounded their film reading desks with framed or mounted illustrations, diagrams, and tables to which they could refer for specific information regarding the size, position, and other characteristics of various anatomic structures. The same practice has been followed by colleagues in other specialties who depend heavily on radiologic evidence in their work. A great service has been provided to both groups through the publication in one volume of some 56 classified groups of radiologic measurements for rapid and accurate reference.

After a wisely included consideration of the distortion factor to be expected when analyzing roentgenograms, the subject matter has been divided into nine anatomic categories, the largest of which deals with the skeletal system. All types of measurement (the location of the pineal body, the time of appearance of various skeletal ossification centers, the size of the heart, the length and caliber of the common bile duct, and the estimation of fetal age on the basis of bone length) are presented in a carefully standardized format. This includes a terse description of the essential examination technique, simple expression of the numerical values involved, and the source of the specific data. Illustrative material from original sources has been augmented extensively by excellent drawings. The book has been so bound that it remains open at any desired point when lying flat. This is a helpful feature when evidence from films is being compared directly with recorded values in the atlas.

The authors have used excellent judgment in selecting the source material to be included. It would have been good, however, to have had other meritorious sources of measurement data included as references by title only, for in several instances material that has been used is deeply interwoven with other published work whose authors have contributed importantly to the subject.

Cholera. By R. Pollitzer, M.D. With chapter on world incidence written in collaboration with S. Swaroop, Ph.D., M.P.H., Chief, Statistical Studies Section, World Health Organization. And chapter on problems in immunology and an annex written in collaboration with W. Burrows, M.D., Professor of Microbiology, University of Chicago, Chicago. World Health Organization monograph series no. 43. Cloth. £ 5; $20; 60 Swiss francs. Pp. 1019, with illustrations. World Health Organization, Palais des nations, Geneva, Switzerland; Columbia University Press, International Documents Service, 2960 Broadway, New York 27, 1959.

The author of this volume has brought together 1,000 pages of up-to-date information on cholera. The 11 listed chapters were printed as separate articles in the *Bulletin of the World Health Organization* prior to this revision. The effects of cholera on a person, population, community, state, nation, and international affairs and all phases of patient medical care, disease control, and prevention are adequately related in this book. Cholera, which Hippocrates described as a disease entity, has been the cause of six pandemics, some of which extended to the United States, in the past century. Cholera was the cause of 1,000 deaths in Calcutta as recently as 1955.

Metabolic Disturbances in Clinical Medicine. Edited by G. A. Smart, B.Sc., M.D., F.R.C.P., Professor of Medicine, University of Durham, Durham. Cloth. $10. Pp. 358, with illustrations. Little, Brown & Company, 34 Beacon St., Boston 6, 1958.

This book is well organized. The subjects covered are interrelated so that one may get the whole picture of the various electrolyte and endocrine problems concerned in a disease entity without jumping from one chapter to another. This book should be useful for the general practitioner as well as the specialist. Each chapter reviews the biochemical changes in the various disease states where there are coexisting metabolic disturbances. Emphasis is more on biochemical changes than endocrine dysfunctions. The illustrations are adequate. The references are excellent and up to date.

QUESTIONS AND ANSWERS

STEROID THERAPY OF CANCER

To the Editor:—*A man, 64 years old, has been found to have pulmonary cancer with metastases to the kidneys and adrenals. Should he be given cortisone or its derivatives or any hormone product? These are expensive medicaments, and there is no hope of cure. Should he receive this medicament through public funds, or should some other less expensive treatment be given to keep him comfortable?*

Francis J. Petrone, M.D., Fall River, Mass.

Answer.—There are no specific indications for the use of cortisone or its derivatives in treatment of patients with carcinoma of the lung. In the patient under discussion, there are two possible indications for use of cortisone as palliative treatment. If the patient is suffering from adrenal insufficiency due to destruction of adrenal tissue by metastases, replacement doses of cortisone would give effective relief. Twenty-five milligrams of cortisone twice daily by mouth would correct the symptoms of adrenal insufficiency if the patient is not under any stress. A larger dosage should be used in a patient who is ill. Although metastases to the adrenal glands are quite common, complete destruction of the adrenal glands resulting in adrenal insufficiency is extremely rare. The diagnosis of adrenal insufficiency can be established by measurement of the blood or urine 17-hydroxycorticoids and by administration of ACTH to determine whether the adrenal glands can be stimulated.

The second possible indication for use of cortisone in patients with advanced cancer might be for relief of symptoms. There is no evidence to indicate that large doses of cortisone produce any significant inhibiting effect on the growth of the tumor. However, relief of pain and improvement in the sense of well-being and in appetite are not infrequently seen in patients in the terminal stages of cancer, unassociated with any inhibitory effects on the tumor itself. These effects of cortisone are usually short-lasting. The relief of symptoms and improvement in well-being may continue for several weeks and thus constitute worthwhile palliative therapy.

"PASSING OUT" SPELLS

To the Editor:—*A 10-year-old girl has had "passing out" spells for the past two years. These at first lasted only a few seconds, but they now last up to half a minute. The child has no memory of the spells. Frequently there is incontinence of urine. Skull x-rays were normal. An electroencephalogram in 1957 revealed diffuse abnormal waves consistent with petit mal convulsive disorder and possibly grand mal variance. Trial therapy with diphenylhydantoin sodium resulted in aggravation of the symptoms. Large doses of vitamin B provided no results. This year the patient was seen by a neurosurgeon who verified the diagnosis of petit mal and prescribed methsuximide, 0.3-Gm. capsules, three times daily. This also appears to aggravate the symptoms, with development of more frequent attacks, considerable irritability, and behavior changes. At the age of about 5 years this child had recurrent fever up to 105 F (40.6 C) and was found to have a kidney and bladder infection. No source of this was ever discovered. She continues to have occasional evening fever of 99 to 100 F (37.2 to 37.8 C) but no urinary symptoms. There have been no operations, hospitalizations, or serious illnesses. Please advise as to diagnostic or therapeutic measures not yet used.*

George R. Farrell, M.D., San Diego, Calif.

Answer.—The urinary infection does not appear to be associated with the neurological problem. Although the febrile episodes may aggravate the convulsive disorder, they cannot be the cause of it. The description of the seizures is not that of major convulsions, since they last such a short time and are described primarily as loss of consciousness. Incontinence of urine does occasionally occur in minor seizures. It is more frequent in psychomotor seizures than it is in petit mal. There is no abnormal activity described in the period of loss of consciousness, and the electroencephalographic findings are more consistent with petit mal than with psychomotor seizures.

Also, the result of the therapeutic trials would suggest that this is not a psychomotor seizure, since diphenylhydantoin sodium might well be expected, in adequate doses, to reduce psychomotor seizures rather than to aggravate them. Indeed, aggravation of the symptoms by diphenylhydantoin suggests that these are petit mal, since this is a common occurrence. A therapeutic trial of trimethadione, be-

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

ginning with 0.3 Gm. per day and increasing to a maximum of 2.7 Gm. per day, if necessary, to control seizures might be indicated. This should be covered with a small amount of phenobarbital, ¼ grain (15 mg.) three times daily, so as to avoid the possibility of inducing major seizures by the use of trimethadione.

The electroencephalogram should be repeated—in the sleeping state as well as in the waking state. There is also the possibility that this child has a progressive degenerative disease, since irritability and behavior changes are developing. However, with the concern of the parents and the undoubted effect of the repeated seizures on the child, particularly if there is severe urinary incontinence, it is quite likely that the irritability and behavior changes are due to environmental pressures rather than to any progressive disease. If therapy with trimethadione is not effective, paramethadione should be tried, and if this also is not effective, then phensuximide.

PSORIASIS THERAPY

To the Editor:—*A lay magazine describes apparent improvement in psoriasis after aminopterin and methotrexate (A-methopterin) therapy. The rationale for such treatment does not seem readily apparent. Is there any basis for it?*

Charles E. Krause, M.D., Caldwell, Idaho.

Answer.—The rationale of the use of aminopterin or methotrexate in psoriasis is not too readily apparent. In psoriasis, it is believed that there is increased keratinization of the epidermal cells as well as increased water vapor loss. One of the effects of aminopterin and methotrexate is to inhibit epithelial proliferation. Both are potentially dangerous drugs and can produce serious toxic effects. These may be ulceration of the buccal mucosa, diarrhea, cramps, thinning of the hair, delayed wound healing, and depression of the number of leukocytes.

DIARRHEA AND LIVER DISEASE

To the Editor:—*For the past few years a woman has had a severe case of chronic diarrhea. There is some palmar erythema. A needle biopsy of the liver showed fatty infiltration and 30% retention of sulfobromophthalein. Are there any records of such liver findings in people past the age of 50 who have no symptoms of any liver disorder?*

B. G. Barentine, M.D., Laurel, Miss.

Answer.—Chronic diarrhea associated with fatty infiltration of the liver and a 30% sulfobromophthalein retention in a person over 50 years of age is suggestive of an intestinal disease with a secondary liver disorder. In order to give a reasonable reply to the above question, it would be necessary to know about the nature of the intestinal disorder causing the diarrhea. Regional enteritis, ulcerative colitis, or a neoplastic disease should naturally receive consideration. Sulfobromophthalein retention of the magnitude described usually indicates more than fatty infiltration of the liver. Such retention is most unlikely in patients with normal livers. More information than is available is needed for an adequate reply to the question.

CUTTING OF VAGUS NERVES AND DIZZY SPELLS

To the Editor:—*A 55-year-old physician underwent a gastrectomy six months ago; at the same time both vagus nerves were cut. During the last four weeks the patient has had recurrent attacks of dizzy spells with nystagmus, nausea, and vomiting. Results of the past-pointing test were positive. The attacks last from 1 to 10 hours. There is no tinnitus or hearing impairment. Could there be any relationship between the cutting of the vagus nerves and the "Ménière-like" attacks?*

Joseph Berberich, M.D., New York.

Answer.—If both vagus nerves are severed (it is doubtful that both were completely severed) there is no feed-back efferently, so, although a branch of the vagus nerve goes to the labyrinth, this should not be the cause of the patient's symptoms. It is more probable that medication postoperatively or the original anesthetic is the cause of the vertigo and nystagmus. It is also conceivable that neurological examination might prove that this patient has Ménière's syndrome, multiple sclerosis, or other neurological disease superimposed on the original condition. This patient should have a neurological survey.

TREATMENT OF SYPHILIS

To the Editor:—*What is the proper oral dosage of penicillin in treating various forms of syphilis? Are the "mycin" drugs any better?*

Arthur F. Edwards, M.D., Los Angeles.

Answer.—I can see no indication for the oral administration of penicillin in the treatment of syphilis. The dosage schedule for injectable penicillin is so well established and the drug is so inexpensive that it would seem pointless to use penicillin orally. In fact, I know of no series of cases reported in the literature in which it has been so used in the treatment of syphilis.

The broad-spectrum antibiotics are nearly all effective in the treatment of syphilis. This has been definitely demonstrated, first with oxytetracycline, and at present tetracycline would certainly be just as effective. One gram a day for from 10 to 20 days should be adequate therapy in most cases. Probably more prolonged administration and higher dosage would be necessary for active general paresis or tabes dorsalis, but these cases today are rare. If medication must be by the oral route, tetracycline reactions, in all probability, would be far less in number and in degree than those possibly encountered with orally given penicillin.

DRIED LIPS

To the Editor:—*A 60-year-old man for 20 years has had drying and cracking of his lower lip. He does not smoke. For the past 10 years he has had artificial dentures. Recently he has had a small malignant growth removed from a corner of the lower lip by radiation therapy. The lower lip is still dry and cracked. Is the origin of this condition known? Is there any therapy?*

M.D., Florida.

Answer.—The query is from a physician in Florida, and presumably the patient has lived there for many years. In this case, dryness of the lower lip is probably due to prolonged exposure to the intense Floridian actinic radiations. The cancer of his lip might also be due in part to the sun's rays. When he is outdoors, his lips should be protected with a sun-screening agent in an emollient base. There are many such products on the market. A person with cheilitis of long standing, with fissures, and especially with a history of an epithelioma, should be examined closely for evidence of other cancerous growths. In some cases it is advisable to have a "stripping operation" of the lip to prevent further trouble. Consultation with a dermatologist or with a head-and-neck surgeon is advisable.

PENICILLIN ALLERGY

To the Editor:—*In the* Southern Medical Journal, *February, 1959, page 186, there is a convincing article on immediate reactions to penicillin. The question has been brought up in staff meeting as to whether scratch tests to detect penicillin allergy might be a cause of promoting allergic responses to the drug. Also, since the form most commonly given is procaine penicillin, would it be necessary to skin test with this, or can one state whether a reaction would be due to the procaine or to the penicillin? We would appreciate advice in this matter from an allergist and an opinion of the medicolegal factors involved in testing for penicillin sensitivity before giving injections.*

Ward B. Breidenthal, M.D., Banner Elk, N. C.

Answer.—There is no evidence from either experience with penicillin or the use of other allergens that scratch tests predispose to an increase in incidence of allergy. Since an immediate type of allergic reaction to procaine is rare (a few equivocal reports of such reactions have been made), one can safely assume that an allergic reaction after administration of procaine penicillin is due to penicillin sensitivity.

The last part of the inquirer's final sentence is unclear. Presumably he wishes to know what the medicolegal responsibility is if the patient is not tested for sensitivity to penicillin and has a severe reaction after its administration. As an allergist who is not an authority on medicolegal aspects of such a case, this consultant would venture the opinion that a thorough inquiry concerning previous reactions to penicillin is more important than skin tests with the substance. A patient who gives a history of previous reactions should be tested by skin and ophthalmic tests if penicillin administration is urgent. Since the value of skin tests in determining the likelihood of systemic reactions is in controversy, this consultant doubts legal liability if no skin test was done, providing that a reliable history indicates that the patient has never received penicillin or that he has never had reactions from its administration.

SUDAN RED TEST FOR FAT

To the Editor:—*Please give information about the Sudan red test for detection of fat in the urine. On two occasions, elderly patients operated on for hip prosthesis have died with what looked like embolic phenomena. Autopsies did not show any cause of death. We are trying to work out a laboratory test that will help to determine whether fat emboli may have occurred.*

Thornton Kell, M.D., Ardmore, Okla.

Answer.—Various azo dyes, including Sudan 2, 3, and 4, have been used as stains for fat. Their ability to stain fat depends on their solubility in oil, and they probably color by means of a physical process. Of the Sudan compounds, Sudan 4 probably is the best for this purpose. It is customarily used as Herxheimer's solution, which consists of 1 Gm. of Sudan 4 dissolved in a mixture of 50 ml. of 70% alcohol and 50 ml. of acetone. When urine is to be stained, a drop of urine is placed on the slide, care being taken to skim the specimen off the surface of the collected urine. An equal amount of Herxheimer's solution is added and the specimen examined under the microscope.

Normal urine does not contain fat, but because fat is found in the urine under a variety of conditions, it is unlikely that a test of this nature will be reliable in determining the presence or absence of fat emboli. Usually, when fat emboli are present in the body, they are found in the lungs. One must be careful to distinguish between fat within and outside of the capillaries, the latter being found normally. Herxheimer's solution may be used in this process of detection. It is important that the tissue never be exposed to alcohol of more than 70% concentration and that all other fat solvents, such as xylene and pure acetone, be avoided. Such tissues usually are fixed in formaldehyde and frozen sections prepared. After these have been placed in 70% alcohol, they are stained with Herxheimer's solution. Slides are mounted in glycerol.

PARONYCHIA OF FUNGOUS ORIGIN

To the Editor:—*Please give an opinion on how best to treat a fingernail which has transverse ridges with other irregularities and pockmarks in the nail and with a raised, rolled area of the skin at the base of the nail, slightly red and slightly painful but never approaching the redness, the pain, or the appearance of acute paronychia.*

J. T. Phillips, M.D., Norton, Va.

Answer.—This nail dyscrasia fits into the clinical picture of paronychia due to the fungus Candida albicans (yeast infection). To confirm this clinical opinion, microscopic examination should be performed. Many of these infections respond to a solution containing 5% nystatin or 8% sodium caprylate. The patient must keep the area out of water and avoid contact with raw fruits and vegetables. Oral administration of nystatin can be used. It is presumed that the possibility of diabetes has been investigated.

STEROID LEVELS IN CHILDREN

To the Editor:—*What are the normal values for 17-ketosteroid and 17-hydroxycorticosteroid determinations in children according to the more popular methods of these determinations?*

G. C. Haskell, M.D., Springfield, Ohio.

Answer.—The plasma 17-ketosteroid level in normal adult men and women averages 60 mcg. per 100 ml. In the newborn infant, the level is equal to or higher than that of the normal adult during the first day of life and falls to low levels by the end of the first week. During infancy and childhood, plasma 17-ketosteroids are practically absent until the onset of puberty, the concentration remaining below 2 mg. until the 8th year. In adult females urinary excretion is between 5 and 14 mg., with an average of 9 mg. in 24 hours; for adult males it is 8 to 22 mg., with an average of 14 mg. The urinary output from the 10 to the 14th day of life is 1.2 to 2.5 mg. per 24 hours and falls to 0.5 mg. by the third to fourth week. There is little change until the 8th year, when there is a gradual rise from approximately 2 mg. to 8 mg. by the 15th year (Wilkins: Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence, ed. 2, Springfield, Ill., Charles C Thomas, Publisher, 1957, p. 306).

The plasma 17-hydroxycorticosteroid level in normal healthy adults varies between 4 and 10 mcg. per 100 ml., and the urinary output, from 3 to 9.3 mg. per 24 hours (Nelson and associates: *J. Clin. Endocrinol.* 11:1021, 1951). In 40 normal children Ely and co-workers (*Pediatrics* 13:403, 1954) found the mean plasma value to be 12.0 and the standard error of the mean ± 1.29 mcg. per 100 ml., a range of 0 to 28.7 mcg. Klein and others (*J. Pediat.* 43:385, 1953) found the mean free corticoid level in children to be 13 mcg., with a standard error of the mean of ± 1.21. After birth, the 17-hydroxycorticosteroid level of the infant's plasma falls to low levels by the third day and then rises to adult levels within 7 to 14 days.

USE OF OLD-FAVORITE REMEDY

To the Editor:—*Use of elixir of iron, quinine, and strychnine, prescribed in our hospital for a number of years, is being challenged by our clinical director, who states that it is outmoded and that newer drugs are better. Several staff members disagree. Its general tonic effect is well known, and I feel, from years of experience, that it does something for the tired-out patient who also has hypertension, especially middle-aged and older persons. It makes them feel better and eat better, and for some reason they lose that tired and always-sleepy feeling. The blood pressure effect is admittedly mild.*

Alfred W. Andreasen, M.D., Danville, Ky.

Answer.—Elixir of iron, quinine, and strychnine has a long clinical history, with wide confirmation of its value as a "tonic." Elixirs and tonics, however, are no longer fashionable in the American hard-driving, highly commercialized therapeutics market; reference to them is found only in European pharmacology textbooks. K. O. Møller, in the most recent edition of his widely used "Pharmakologie als theoretische Grundlage einer rationellen Pharmacotherapie" (New York, Grune & Stratton, Inc., 1947) fully describes the significant therapeutic indications for strychnine as a tonic. Bitterness of both quinine and strychnine even in the flavored elixir is enough to give a stimulus to appetite. Strychnine does facilitate ganglionic nerve transmission. Quinine has wide effects, often helping to stabilize cellular function, particularly with reference to water and electrolyte balance. It is well known that iron is useful in chronic debilitating conditions, particularly where iron deficiency may be part of a picture of anemia.

It would seem that the tried and tested tonic value of elixir of iron, quinine, and strychnine deserves continued recognition. Its effects are not dramatically quick as in the case of many new drugs which seem to have a stimulating effect on the central nervous system, but it does improve the over-all condition in tired middle-aged or older persons, in patients convalescing from debilitating disease, and in conditions where there is a let-down feeling or mild depression.

WASHINGTON NEWS

Study Group Urges Medical
School Expansion . .
Court Rules on Medical Partnership . .
HEW Writing Rules . .

FEDERAL REPORT ON MEDICAL EDUCATION NEEDS

A broad program of federal, state, and private aid to boost the number of physicians and medical schools was recommended by a special advisory group to the Public Health Service, officially called the surgeon general's group on medical education, which declared that expansion of existing medical schools and establishment of new ones "must be greatly accelerated."

Contending that the present ratio of physicians to population (about one physician to every 740 persons) is the "minimum essential to protect the health of the people," the 23-member consultant committee recommended that by 1975 medical schools graduate 11,000 physicians annually, 3,600 more than now. Current plans for expansion of schools and facilities "would not be adequate to maintain the current ratio of physicians to population," the committee said in a 95-page report to Surgeon General Leroy E. Burney.

Among other proposals, the group suggested federal grants-in-aid to help construct new medical schools, federal scholarship assistance for medical students, and community and private help to maintain high training standards.

The advisory group, headed by Frank Bane, former executive director of the council of state governments, has been studying the problem for more than a year. Congressional action on proposals to assist medical schools were held up last session until the report could be completed and the administration could make its own recommendations, if any, based on the report.

One of the major legislative steps called for was a 10-year program for expanding medical school facilities. Under this "[illegible]" the federal government would appropriate funds on a matching basis (that is, with a nonfederal source putting up the same amount) for expansion and improvement of existing schools and construction of new schools of basic sciences, new four-year medical schools, and the necessary teaching hospitals.

In addition, according to the report, "there should be more generous public and private support for the basic operations of medical schools. This support must come from many sources, including state and local appropriations, endowments, gifts and grants, universities, and reimbursements for patient care."

As for federal research grants, the Bane committee said, these should cover the full indirect costs so that medical schools are properly reimbursed for the contribution of medical education to medical research.

Commenting on these proposals, the study group declared, "Probably the greatest immediate obstacle to expanding the nation's medical educational capacity in existing schools and in the development of new schools is the problem of financing the needed facilities. In addition, many schools are beset by problems of attempting to carry out teaching activities in overcrowded and obsolescent buildings despite the considerable construction which has taken place in recent years. A program to meet the accumulated needs is urgently required."

The consultant group is convinced that the nation's supply of physicians will continue to lag behind the needs created by an increasing population, unless the federal government makes an emergency financial contribution on a matching basis toward the construction of medical school facilities. "Only with such a federal stimulus will adequate funds become available for needed construction."

Other recommendations of the committee were as follows.

Medical students

Aggressive action by foundations, individual persons, industry, and voluntary agencies to obtain additional private support of medical students, including both low-cost loans and scholarships for persons who otherwise would be unable to finance a medical education.

State loans, grants, or scholarships for selected medical students.

Federal educational grants-in-aid for medical students.

Special consideration under the federal student loan program "in order that medical students may receive loans in proportion to their urgent needs for assistance."

Medical school standards

Increases in facilities and students "should be made in a manner which protects the quality of medical education."

Greater attention must be given to the problems of existing schools whose educational plants or programs are now inadequately financed (estimated at 15% of medical schools).

"Schools should consider the effect of unreasonably restrictive admission policies on the quality of their students and the need for a student body with diversified interests and background."

Evaluation should be made of experiments to shorten the period of medical training.

Planning

Medical schools should make every effort to increase enrollment consistent with the maintenance of good educational programs.

When federal funds become available to aid medical education, a national committee should be established to advise the surgeon general on the administration of such funds—the work of the group should be closely coordinated with that of the National Advisory Council on Health Research Facilities and the Federal Hospital Council, which are concerned with administering federal grants for research facilities and hospital construction.

The study group made similar recommendations for dentists and warned there would be a shortage of dentists unless such programs are undertaken.

In addition to Dr. Bane, members of the study committee are Robert C. Anderson, Ph.D., director, southern regional education board; Fred C. Cole, Ph.D., president, Washington and Lee University; Edwin L. Crosby, M.D., director, American Hospital Association; Ward Darley, M.D., executive director, Association of American Medical Colleges; Harold L. Enarson, Ph.D., director, western interstate commission for higher education; Alvin C. Eurich, Ph.D., vice-president, fund for the advancement of education; Harold Hillenbrand, D.D.S., secretary, American Dental Association; Norvin C. Kiefer, M.D., chief medical director, Equitable Life Assurance Society of the United States; Vernon W. Lippard, M.D., dean, Yale University School of Medicine; Clayton G. Loosli, M.D., dean, University of Southern California School of Medicine; John McK. Mitchell, M.D., dean, University of Pennsylvania School of Medicine; Emory W. Morris, D.D.S., president, W. K. Kellogg Foundation; Julian P. Price, M.D., member, Board of Trustees, American Medical Association; I. S. Ravdin, M.D., vice-president for medical affairs and professor of surgery, University of Pennsylvania; John G. Searle, president, G. D. Searle & Co.; Marion W. Sheahan, deputy general director, National League for Nursing, Inc.; Very Rev. Robert J. Slavin, O.P., Ph.D., president, Providence College; Charles E. Smith, M.D., dean, School of Public Health, University of California; Morris Thompson, Sc.D., president, Kirksville College of Osteopathy and Surgery; Edward L. Turner, M.D., director, Division of Scientific Activities, American Medical Association; and Douglas E. H. Williams, executive secretary, Dunbar Community Association, Inc.

TAX RULING ON MEDICAL PARTNERSHIPS

The U. S. Tax Court held that a physician and his wife may form a partnership for tax purposes provided the wife truly acts as a partner in the business. The decision was handed down in a case involving a Seattle radiologist, the late Dr. Harold E. Nichols, and his wife Beulah. The Internal Revenue Service contended the partnership was invalid and sought to collect back taxes. However, the tax court held that Mrs. Nichols performed all of the work necessary to qualify as a full-fledged partner and rejected the government's suit.

In another decision, the court said that the cost of dancing lessons suggested by a physician for therapeutic purposes are not deductible in most cases as medical expenses.

HEW SPELLS OUT WRITING RULES FOR EMPLOYEES

Arthur S. Flemming, Secretary of Health, Education and Welfare, announced a new policy governing outside writing activities of the agency's 60,000 employees, many of whom are physicians and scientists in medical fields.

Unless there is a real or apparent conflict of interest with the government, an employee is free to engage in such work, said Flemming. However, he said the employees "must not even have the appearance of acting in private capacities contrary to the public interest they serve in their government positions."

The secretary said there is no disposition to censor and that the heads of the various operating agencies, including the Public Health Service and the Food and Drug Administration, will make the decisions in individual cases. Appeals may be carried to the HEW Secretary.

Flemming told a press conference that the new program will provide maximum opportunity to engage in this field consistent with laws and regulations. He noted that it was important for scientists to continue to publish articles in the line of duty.

Previously there had been no outside writing provisions to guide HEW employees, Flemming said, disclosing that the new rules will be incorporated into a manual.

Where information is secured that is available to anyone and an employee writes on his own time and with his own materials, without any other restrictions on him, then he is free to engage in the activity. "Conflict of interest" is the real test, according to Flemming.

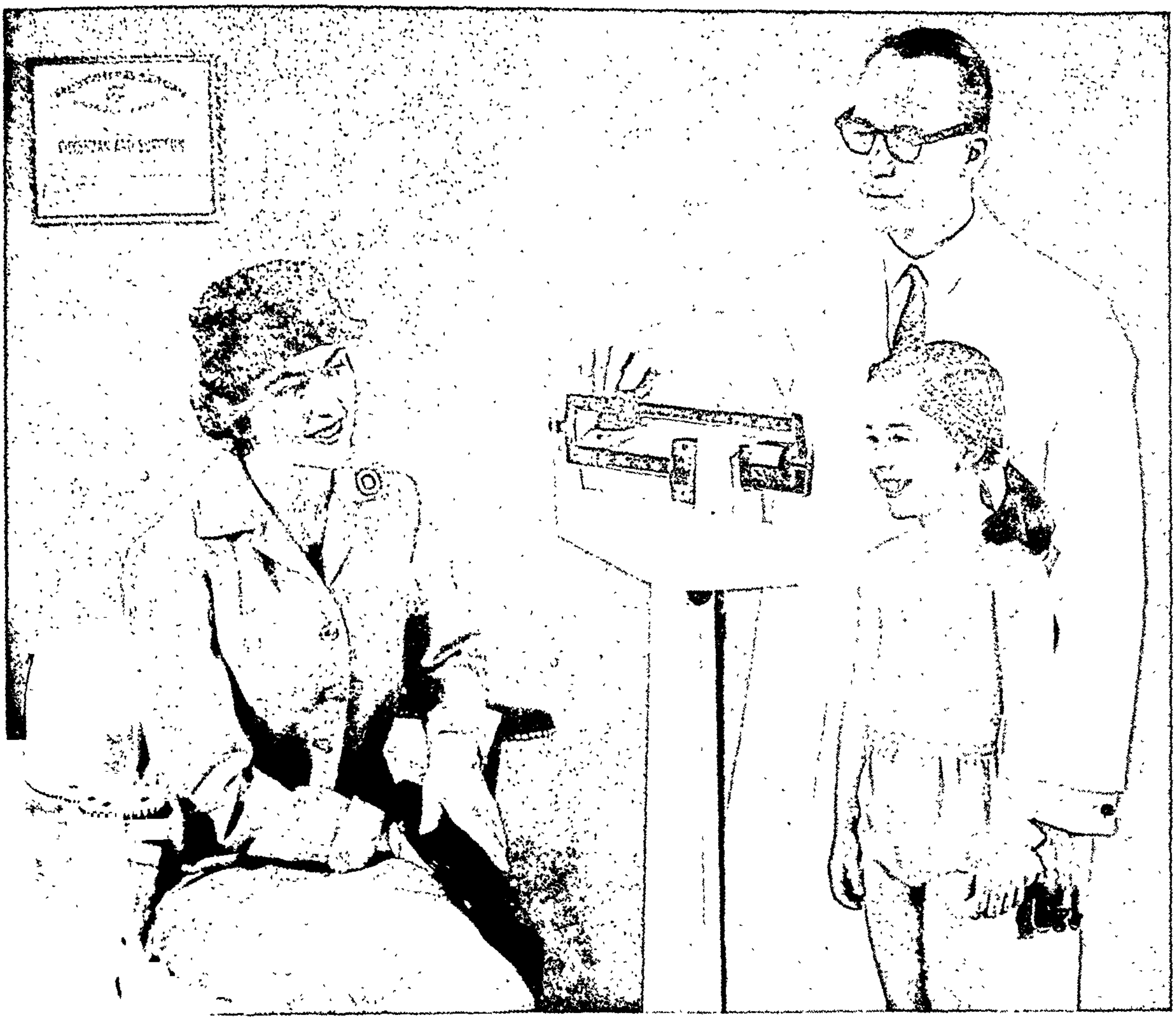
The new policy stemmed from a controversy earlier this year over the outside writing of Dr. Henry Welch, chief of FDA's antibiotics division. Flemming told the news conference that Dr. Welch had resigned from most of his private editorial positions.

Flemming commended Dr. Welch as an outstanding scientists who had done nothing contrary to the best interests of government. He pointed out that the outside work was undertaken only after Dr. Welch had consulted with his superiors and obtained their approval.

Dr. Welch resigned his editorial positions with the publications *Antibiotics and Chemotherapy*, *Antibiotic Medicine and Clinical Therapy*, and *MD* magazine. At the same time, Medical Encyclopedia, Inc., the publishing house in which Dr. Welch has a financial interest, will discontinue publishing "Antibiotics Annual."

MISCELLANY

The Veterans Administration reported that physicians at the Washington, D. C., and Richmond, Va., VA hospitals have announced successful results in clinical trials of a new drug used for lowering high blood pressure. The drug, guanethidine, had a potent effect in reducing high blood pressure, similar to the effects of ganglionic-blocking drugs but without their undesirable reactions.



Underweight Children Gain and Retain Weight with Nilevar®

One of the most convincing evidences of the anabolic activity of Nilevar, brand of norethandrolone, has been its ability to improve appetite and increase weight *in poorly nourished*, underweight children.

A highly important feature of the weight gain thus produced is that it is not ordinarily manifested by deposition of fat but as muscle tissue resulting from the protein anabolism induced by Nilevar.

Anorexia and "Weight Lag" Study—Brown, Libo and Nussbaum have reported* consistent and definite increases in rate of weight gain in eighty-six patients, ranging in age from 7 weeks to 15½ years. This beneficial action of Nilevar was observed in the patients with organic and traumatic disorders as well as those whose only complaints were poor appetite and/or persistent failure to gain weight.

In this study, the weight gained was not lost after discontinuance of Nilevar therapy although many patients did not continue the sharp gains effected by the drug.

The authors are of the opinion that Nilevar is a highly useful anabolic agent for influencing weight gain in underweight children.

When Nilevar is administered to children a dose of 0.25 mg. per pound of body weight is recommended and *continuous dosage for more* than three months is not recommended.

Nilevar is supplied as tablets of 10 mg., drops of 0.25 mg. per drop and ampuls of 25 mg. in 1 cc. of sesame oil. Further dosage information in Searle Reference Manual No. 4.

G. D. Searle & Co., Chicago 80, Illinois. Research in the Service of Medicine.

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*Brown, S. S.; Libo, H. W., and Nussbaum, A. H.: Norethandrolone in the Successful Management of Anorexia and "Weight Lag" in Children, Scientific Exhibit presented at the Annual Meeting of the American Academy of Pediatrics, Chicago, Oct. 20-23, 1958.

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

November

Academy of Medicine of Cleveland Seminar on Recent Advances in Diagnosis and Therapy of Malignant Disease, Cleveland, Nov. 18-19. Dr. H. S. Van Ordstrand, 2009 Adelbert Rd., Cleveland 6, Chairman.

American Academy for Cerebral Palsy, Statler Hilton Hotel, Los Angeles, Nov. 30-Dec. 2. Dr. Glidden L. Brooks, Brown University, Providence 12, R. I., Secretary.

American Association of Blood Banks, Edgewater Beach Hotel, Chicago, Nov. 4-7. Dr. John B. Alsever, Southwest Blood Banks, 1211 W. Washington St., Phoenix, Ariz., Secretary.

American College of Chest Physicians, Dallas, Texas, Nov. 29-30. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Secretary.

American Medical Women's Association, Arlington Hotel, Hot Springs, Ark., Nov. 12-15. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

Association of Military Surgeons of the United States, Mayflower Hotel, Washington, D. C., Nov. 8-11. Lt. Col. George M. Beam, AUS, Ret., Suite 718, New Medical Bldg., 1726 Eye St., N. W., Washington 6, D. C., Executive Secretary.

Central Society for Clinical Research, Drake Hotel, Chicago, Nov. 6-7. Dr. Austin S. Weisberger, 2065 Adelbert Rd., Cleveland 6, Secretary.

Chicago Heart Association, Symposium on Cerebral Vascular Diseases, Knickerbocker Hotel, Chicago, Nov. 7. Dr. C. Bruce Taylor, c/o Chicago Heart Assn., 22 W. Madison, Chicago 2, Chairman.

Conference on Electrical Techniques in Medicine and Biology, Sheraton Hotel, Philadelphia, Nov. 10-12. Dr. Herman P. Schwan, Moore School of Electrical Engineering, University of Pennsylvania, Philadelphia, Chairman.

District of Columbia, Medical Society of, Statler-Hilton Hotel, Washington, D. C., Nov. 23-25. Mr. Theodore Wiprud, 1718 M Street, N. W., Washington 6, D. C.

Gerontological Society, Inc., Statler Hotel, Detroit, Nov. 12-14. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Administrative Secretary.

Illinois Academy of General Practice, Morrison Hotel, Chicago, Ill., Nov. 9-12. Dr. H. Marchmont-Robinson, 14 E. Jackson Blvd., Chicago 4, Executive Secretary.

International College of Surgeons, Second Western Regional Meeting, Stardust Hotel, Las Vegas, Nev., Nov. 22-24. Dr. F. M. Turnbull Jr., 1930 Wilshire Blvd., Los Angeles 57, Secretary-Treasurer.

Inter-Society Cytology Council, Statler-Hilton Hotel, Detroit, Nov. 19-21. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secretary-Treasurer.

Michigan Academy of General Practice, 13th Annual Fall Postgraduate Clinic, Sheraton-Cadillac Hotel, Detroit, Nov. 11-12. Dr. F. P. Rhoades, 970 Maccabees Building, Detroit 2, Convention Manager.

National Proctologic Association, Chicago, Nov. Dr. George E. Mueller, 59 E. Madison, Chicago 2, Secretary.

National Society for Crippled Children and Adults, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

Puerto Rico Medical Association, Santurce, Nov. 24-28. Mr. J. A. Sanchez, Box 9111, Santurce 29, Puerto Rico, Executive Secretary.

Radiological Society of North America, Inc., Palmer House, Chicago, Nov. 15-20. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary-Treasurer.

San Diego Academy of General Practice, Hotel Riviera, Las Vegas, Nev., Nov. 12-14. For information write: Dr. Harold Peterson, 5950 El Cajon Blvd., San Diego 15, Calif.

Society for the Scientific Study of Sex, Barbizon Plaza Hotel, New York City, Nov. 7. Mr. Robert V. Sherwin, Suite 704, 1 E. 42nd St., New York 17, Executive Secretary.

Southern Medical Association, Atlanta, Nov. 16-19. Mr. V. O. Foster, 2601 Highland Ave., Birmingham 5, Ala., Executive Secretary-Treasurer.

Southern Thoracic Surgical Association, Edgewater Gulf Hotel, Edgewater Park, Miss., Nov. 19-21. Dr. Hawley H. Seiler, 517 Bayshore Blvd., Tampa 6, Fla., Secretary.

Southwestern Medical Association, Roswell, N. M., Nov. 5-7. Dr. Russell L. Deter, 1501 Arizona St., El Paso, Texas, Secretary.

Western Surgical Association, The Broadmoor, Colorado Springs, Colo., Nov. 19-21. Dr. John T. Reynolds, 612 N. Michigan Ave., Chicago 11, Secretary.

December

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bldg., Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York City, Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, Secretary.

American Rheumatism Association, Henry Ford Hospital, Detroit, Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

First Annual Graduate Medical Education Conference-Residency Training Program, Univ. of Pennsylvania, Philadelphia, Dec. 3-4. Dr. Alfred S. Frobese, Graduate School of Medicine, U. of Pennsylvania, Philadelphia 3, Chairman.

Medical Society of the United States & Mexico, Valley Ho Hotel, Scottsdale, Ariz., Dec. 2-4 (followed by two-day session Desert Inn, Las Vegas, Nev.). Dr. A. H. Tallakson, 2025 N. Central Ave., Phoenix, Ariz., Convention Co-Chairman.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly in Anesthesiology, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. John R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 28-30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executive Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Dr. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretary.

Western Society for Clinical Research, Carmel-by-the-Sea, Calif., Jan. 28-30. Dr. William N. Valentine, U. of California Medical Center, Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. George Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Inn, Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Medicine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbour, Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tower, Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, Feb. 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executive Director.

American College of Surgeons, Sectional Meeting for Surgeons and Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chicago, Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York 19, Executive Secretary.

California Medical Association, Ambassador Hotel, Los Angeles, Feb. 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Executive Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18-20. Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Canada, Secretary.

Congress on Medical Education and Licensure, Palmer House, Chicago, Feb. 7-9. For information write: Council on Medical Education and Hospitals, American Medical Association, 535 N. Dearborn St., Chicago 10.

National Association of Methodist Hospitals and Homes, Deshler Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 740 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern California, Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Los Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Ben Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University of Texas, Houston, Feb. 25-27. For information write: University of Texas M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Hotel, Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust St., Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chicago, Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secretary-Treasurer.

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MEDICINE IN THE TEACHING HOSPITAL OF TODAY AND TOMORROW

Walter Bauer, M.D., Boston

TO SERVE as president of the Association of American Physicians is both an honor and a privilege. My most awesome duty has been this presidential address. I found it an even more lonely task than had been expected. Not until my thoughts and ideals were shared with some of my colleagues did the experience become rewarding. On reviewing the pace of human progress and the many resulting problems, one becomes increasingly aware that the potentiality for future progress has never been so great. There is, however, a wide disparity between achievement and potential. It is this theme that I wish to develop.

We are living in an exciting period of great change and transition. Contemporary political, cultural, economic, and scientific upheaval is affecting every facet of human existence—and in no sphere, I submit, are these forces more complexly interwoven than in the science, or art, or profession of medicine in the world of today. Yes, the circumstances of daily life are changing more rapidly than they have ever changed before in man's experience. We must reckon with these many forces if we are to supply stability of purpose to our teaching hospitals. We must also be promptly and delicately responsive to changes in our environment as well as to changes in objectives.

I should like to discuss certain aspects of this problem as they concern medicine, for I feel deeply that some of our difficulties may be unique to our times and that the moment is at hand for forthright consideration of how best to meet them now and in the future. I will address myself to some of the problems now facing the university teaching hospital and its department of medicine.

Good medical care must still depend on the dedicated and well-trained physician. The integration of medicine depends on the integration of medical teachers. The educational experiment here described involved the creation of integrated units within a teaching hospital, each unit being a miniature department of medicine made up of full-time and part-time physicians, clinical investigators, and, in some instances, basic scientists. The units are devoted to such fields as hematology, gastroenterology, and cardiology, and the arrangement is not to be confused with the division of a hospital into arthritis wards, gastroenterology wards, pulmonary disease wards, and so on. The unit team plan provides superb opportunities for broadening the viewpoints of medical students and house staff alike. Teaching is improved, research is stimulated, and the purpose of the whole enterprise, to give the individual patient the best possible care, is constantly kept in view.

Jackson Professor of Clinical Medicine, Harvard Medical School, and Chief of the Medical Services, Massachusetts General Hospital.
Presidential address, read before the Association of American Physicians, Atlantic City, May 5, 1959.

We must keep in mind the special role of the teaching hospital in contemporary medicine. Its function is a creative one. Here, new physicians are trained and graduated. Here, the character and content of medical practice are continuously reshaped as new researches are conducted and new ideas are conceived and tested. And here, last but not least, the patient is cared for in a manner that not only gives him the best that medicine has to offer but also displays a standard and style of care that students and house staff may strive to emulate in the years beyond their training. This should be patient care in medicine's grand tradition, embodying humanity, wisdom, dignity, and compassion. But it is something more; it is razor-edged scientific analysis, probing, observing, recording, doubting, alert to every aberration—from the patient's demeanor to the enzymes in his serum. The teaching hospital does indeed have a special creative role, placing on it responsibilities, both grave and inescapable. What we do and think in our teaching hospitals will influence the thought and practice of our colleagues everywhere and, in turn, the health and happiness of our generation.

Current Problems

The great problem we now face is: How can we provide and maintain a properly balanced program of patient care, teaching, and research in the face of the torrential outpouring of new knowledge? Much of this knowledge has clear relevance for medicine, and more could have relevance if the right person were on hand to perceive and exploit its latent importance. Problems never come earmarked as problems. How, then, can we investigate an unknown in medicine if it has to be approached in biochemical terms by men who must both recognize a clinical problem and conceive a biochemical solution? If we are to promote meaningful and competent research at the more fundamental levels of biological organization, how can we simultaneously imbue our students with the chief humanistic aim of medicine—which is, that the patient's interest comes first and the investigator's second? How can we best integrate the new movement in scientific medicine with the work and thought of our experienced clinicians, who may be alienated by its esoteric techniques and minute concern with the capers of carbon atoms?

These are the questions to be answered and the problems to be faced. Few would deny the major premise that a new scientific revolution is upon us. Starting soon after World War II, there has occurred an incredible output of basic biological research in fields adjacent to or potentially adjacent to medicine. The factors inciting this revolution—the advent of radioactive isotopes, perfection of chromatographic procedures and methods of protein purification, increased financial support of research, etc.—are beyond the scope of this discussion. Suffice it to say that many of our young physicians have participated in this development. Some of them have had a period of formal scientific training at our universities or similar institutions. Others have somehow managed to train themselves in scientific disciplines even while working in clinical areas. This is mirrored in our medical journals and the content of our research meetings—fully illustrated by yesterday's program, where we noted that "the syndrome" is giving way to what might be called "the gospel according to Saint Geiger."

We are standing in the middle of what might reasonably be called a blizzard of scientific progress. The rate at which progress is being made has led to increasing difficulty in keeping abreast of the published reports of that progress. The inevitable consequences have been an increase in specialization, a tendency toward separation of practice from research, and, as some would say, the invasion of one field by persons whose backgrounds and training have been in other areas. In addition to this increase in specialization, there has arisen an increasing difficulty of communication not only between persons in different scientific disciplines but also between persons within a given field. How, in the face of these difficulties, can we achieve and maintain a high standard of patient care, teaching, and research—a *modus operandi* which will enable us to preserve the unity of the whole of internal medicine? How can we mount this whirlwind and make it take us where we want to go? I am sure there are no right answers to these questions—that is, no answers that are right for each department of medicine or for each member of such a department.

An Experiment in Medicine

The major purpose of our annual meeting is to consider together the results and implications of experimental medicine. Because of this, I am encouraged to outline for you, in the form of a progress report, the results of an experiment in progress at the Massachusetts General Hospital—an experiment in how to accommodate ourselves most effectively to meet the challenges and opportunities of present-day academic medicine. The approach which I shall outline is neither new nor unique, and the validity of its results can never be unassailably fortified with the armor of standard deviations and chi squares. Nevertheless, I am convinced that this experiment or some parallel approach must be vigorously pursued in every teaching hospital.

This program has been based on two general premises. The first is that specialization is necessary and that it is here to stay. Himsworth has phrased this point aptly:

> The present situation has arisen because medical knowledge has grown to such an extent that it is no longer, and never again will be, within the capacity of any individual man to master more than a small fraction of it. Specialization has become a necessity. To decry this not only ignores fact; it is to deny the very means that have made our recent progress possible. Specialization is a natural phenomenon. It is comparable in human affairs to differentiation of function in biology. . . . It is the same with human organizations.

Specialization holds out to them—be they intellectual or social—the promise of vast extensions in power; but it does so only on condition that integration keeps pace with specialization.

According to Himsworth, then, the difficulties arise not from specialization but from failure of integration. This leads to our second general premise—that integration must exist both among and within individual persons, particularly those key men who lead team efforts. Unless it does, the results may be disappointing.

Units in Medical Service.—Our medical service is composed of autonomous units, each covering one of the specialties of internal medicine. We have a hematology unit, a gastroenterology unit, a cardiology unit, and various others—12 in all—covering most of the categories into which internal medicine has been divided.

In medicine, as in all of biology, we are primarily concerned with the details of structure and its relationship to function. Therefore, one may well ask: "What is the composition of these specialty units, what responsibilities do they assume within the department of medicine, and how do their structures help them to attain their avowed goals?"

Each unit is a group, of variable but workable size, made up of full-time and part-time physicians, clinical investigators, and, in some instances, basic scientists. Dr. Dana M. Atchley, in a personal communication, has written as follows: "I think we should speak of the 'clinical scientist' and the 'basic scientist' because no clinician these days can be a good clinician if he is not a scientist in his attitudes and training."

Each unit must serve as a miniature department of medicine, dedicated to total competence within its designated area of interest. The sweep of its activities must carry from basic laboratory research to the imaginative application of its discipline to the cure of the ill. This is no less than an injunction to these units to maintain a high standard of excellence in mastering the skills of their specialty areas, in applying these skills effectively, in the acquisition of new facts, and in the teaching of its discipline to other students of medicine.

Functions of the Units.—Where can the harassed chief of a medical service find a physician to carry out all of these activities effectively within a specialty area? In American medicine—the answer comes back clearly—it is "nowhere." A specialty unit can no longer be the lengthening shadow of one gifted person, miraculously adapted to the laboratory, the lecture hall, and the clinic. Basic laboratory research in all medical specialties obsessively demands the devoted attention of first-rate minds for maximal returns. Alternatively, seasoned clinical wisdom based on critical evaluation of experience, which is the hallmark of the excellent physician, cannot be acquired as a gratuitous by-product of laboratory research. Proficiency in clinical medicine is painfully acquired and must be constantly cultivated or else it degenerates into the marketing of shopworn sophistries. Faced with this dilemma, we have accepted the fact that it is the unit, not the person, which must responsibly insure the pursuit of medicine in its broadest sense as an area of both theoretical and applied biology.

How is this carried out in practice? One of our smallest units, for example, is composed of physicians who have had extensive training in organic or biological chemistry, physicians who have had experience in the physiological and metabolic techniques of classic clinical research, and clinicians in private practice who maintain an interest in this medical specialty. The weekly activities of this unit attempt to correlate these various approaches. There is a seminar at which the basic scientific foundations of the discipline are explored, led by either a member of the unit or a guest speaker. The unit holds its own weekly "grand rounds" at which the clinical problems of one or two patients are explored in detail, attempting the most precise scientific analysis of the illness, its pathogenesis, and treatment. Finally, there is a specialty clinic and a consultation round at which a large number of specific clinical problems are met in the daily evaluation and care of patients. All of these functions are attended by students and all members of the unit, irrespective of their primary interests. Each makes his major contribution within the area of his greatest competency but serves further to challenge the accuracy and significance of observations and traditional teaching of the other areas of the discipline.

One of the larger groups, the connective tissue unit, is comprised of persons representing a wide variety of backgrounds and disciplines, who share a common interest in the connective tissue, its components, and its diseases. Senior members include practicing physicians, four clinical investigators, a biologist, a protein chemist, and an organic chemist interested primarily in the carbohydrates. Together with a number of clinical and research fellows and students, these persons share the responsibilities previously mentioned and, of course, conduct their own research.

The physician members of each unit also visit on the general medical wards and participate in the teaching of general internal medicine to second-year, third-year, and fourth-year students. Each of the senior investigators is responsible for determining the direction of, and conduct of, his own research work. Collaborative research problems are undertaken when they spring from common interest.

To present one's work and ideas, either formally in a conference or informally over a cup of coffee, before this group of persons whose interest is keen and whose backgrounds are so varied, has proved to be a privilege which each member values above all others.

Value of Unit System.—Is such a unit just another malignant example of the "togetherness" so increasingly evident on the contemporary American scene? Does any interreaction occur when the scientist and the clinician are brought together? Here lies the crux of the problem. For the successful functioning of this system, we have attempted to appoint a particular type of man to head each unit—a man who by some means has managed to plant a solid foot in a scientific discipline beyond the scope of clinical medicine, generally in biochemistry, biophysics, or physiology. I have the strong conviction that in the careful selection of unit heads lies the key to the success of this plan. By combining clinical medicine and basic science in their training, and by displaying superior competence in both fields, they represent a new breed of physician. Just as the biochemist once was a strange breed, trained in both chemistry and biology, he managed, nevertheless, to survive and flourish. Likewise, this new breed of physician, born of necessity, the product of modern medicine's complexity, will also survive and flourish. They will flourish along with their conventionally trained colleagues—in teaching hospitals where, we hope, their unique viewpoint will promote strong leadership and progress. They will respect the achievements of the clinicians and talk their language. Their scientific background and training should enable them to produce research of competence, comparable to that of the nonclinically trained scientist.

It is true that such men are hard to find, and a chief of medicine who wishes to develop a unit system of this sort must take the time and make the effort to find, to nurture, and to encourage this small but important group of young physicians who show promise of development in this direction. This may be one of his most important responsibilities. Equally important, he must also recruit the much-needed quota of able part-time physicians—clinicians who, because of previous training, wish to maintain an interest in a given medical specialty, as well as to participate in the teaching of students and house staff. He must also do everything in his power to attract top-flight scientists.

Through the efforts of such people, it should be possible to mount a team effort that will develop cohesion and direction. We, at the hospital, like to think of each unit as a balanced one, with due attention paid to all levels of work. Each member should select and occupy his own position in the spectrum, from pure science to clinical medicine, and should command respect for his abilities and accomplishments. We would like to believe that in such units the whole may be greater than the sum of its parts. There should be little room in such units for suspicions and condescending attitudes so often marring the relationships between scientists and clinicians.

In this way, viewpoints can be shared, horizons broadened, and opportunities increased for individuality and self-development. By cooperative effort, members of a unit may take time off in sabbatical leaves or other changes of pace, so necessary for the maintenance of a fresh point of view. In this way, a better appreciation of the many roads that lead to medical knowledge may be achieved. It is already becoming clear from our experience with this plan how exciting and fruitful the results of such team efforts can be when guided by the sort of men about whom I have been talking.

Relationship of Units.—You may well ask how these units relate to one another and function as an integrated department of medicine. The head of the department meets with the chiefs of units at stated intervals. Here, problems are aired with candor and sometimes heat. This not only helps us in effecting unity of purpose in the care of patients and teaching but also familiarizes each unit with the research interests and aims of the others. These and other regularly held exercises help to further our common objectives without encroaching on individuality of expression or action.

Such a department of medicine has all the specialty subdivisions in medicine for purposes of investigation and teaching, yet the foundation of internal medicine is the general medical ward in which all of the various specialty members participate in the care of the sick, no matter whether the patients have the diseases in which they are well versed. It is the general medical ward that is the basic area of integration, both of the person and of the discipline itself. I, personally, deplore the departments of medicine that have arthritis wards, gastroenterology wards, pulmonary disease wards, and others, and distribute their patients on admission to these specialized services. In my opinion, medicine cannot be done that way in the last analysis. It can be and must be studied in the specialty areas, but the care of the patient in the final integration has to be done by an internist working in a general medical service. I emphasize this point because there is a trend in the other direction in the United States and abroad.

Effective Hospital Program

We return, then, to our original question: How can a teaching hospital effectively carry out a program of medical care, teaching, and research? How does the integration achieved in the units help in the pursuit of these three goals? Let us consider them one by one.

Teaching.—As for teaching, the exposure to the unit teams provides superb opportunities for building into medical students and house staff a broad point of view. We have long since conceded that the undergraduate phase of medical education can no longer turn out physicians ready for the practice of medicine. It has to be satisfied with the building of general competence, leaving the acquisition of special knowledge and skills to the graduate training program—especially residency training. Much has been written in recent years about integrating the medical curriculum. Is it not reasonable to expect that this goal will be more closely approached if our teachers are better integrated? This must surely be a prerequisite for the success of an integrated curriculum, no matter how carefully it is planned.

Education is a simple process. It begins when two people of different life experiences meet and talk. It is this communication between those who are willing to learn from one another which is the essence of the educational experience. Obviously, we cannot teach our patients all of medicine. What we can teach them, however, is the habit of being self-taught. As has recently been said, "It is our job as educators to see to it that our students, on graduation, be not rifle bullets, constantly decelerating, but self-propelled missiles."

Research.—What about research—such an essential component of the modern university medical center? As physicians dedicated to the prevention and treatment of disease, we are vitally interested in furthering this goal. This we can attain by a better understanding of our patients, their diseases, their disturbed physiology, the biology of the involved tissue, and the chemistry and/or biology of potential etiological agents. Having assumed responsibility for teaching, we must imbue our students with an intellectual curiosity at all these levels. Finally, what better antidote for the dangers of cant and dogmatism than research? The unfounded statement, the unsupported conviction, or the traditional belief are not likely to survive long in the questioning attitude engendered by research. To paraphrase an Elizabethan dramatist—research does make better doctors of us all.

Most medical research can be carried out more effectively within a teaching hospital than in a research institute devoid of an association with medical care and teaching. This is obviously true for traditional clinical research, of whatever variety. It is becoming increasingly evident that this is also true for the more basic scientific disciplines. In recognition of this fact, research institutes such as the Rockefeller Institute and the National Institutes of Health have seen fit to provide themselves with hospital facilities to further their research programs. Within the hospital setting the scientist is made constantly aware of the problems involved in medical care while being stimulated by association with students and physicians concerned with the validity and application of medical knowledge. It is our hope that more scientists will do their research in hospitals. If they do, the unit system may be the means by which they will become aware of the unsolved problems of clinical medicine. We also hope that our units will attract scientists to their units, for this would add as much to medicine as it would to science.

Fundamental research should be an integral part of the modern teaching hospital and can no longer be considered a luxury. The full-time scientist in the hospital must be regarded as the professional equal of the clinician and not his handmaiden. We trust that some of these important men will wish to remain permanently in the hospital research setting. Undoubtedly, some will return to other academic departments in medical schools and universities, carrying with them a new awareness of the applicability disciplines to medicine.

Medical Care.—Finally, last to be mentioned but surely not least, we come to patient care—the goal and purpose of the whole complicated enterprise. This remains our primary concern. There are many opportunities in this area for self-delusion and cant. We must impress on our students and house staff the importance of thinking of each patient as a whole human being, a man or a woman of certain social and economic background, with hopes and fears and feelings of guilt and pride. Students so indoctrinated will be mindful of the fact that all the symptoms of a given patient are not necessarily due to a genetically determined enzyme deficiency, however crisply revealed before our eyes by the incontestable techniques of biochemistry. Unless our students are so trained, they will not bring to bear in future years the wisdom and vision needed in helping patients attain better health and more happiness.

We must face this problem honestly. We must avoid the pitfalls of lip service and inconsistency. Here again the unit system can be of help. Beyond the scope of any single person, it has the potential for demonstrating that no sharp boundaries can be drawn between the scientific analysis of disease and the compassionate care of the sick. We trust that unit chiefs will always keep clearly in mind that the primary concern of a teaching hospital is the care of the sick and that it is within this framework that the activities of the unit must be carried out. For the same reasons they should be aware that the definition of good medical care is as elusive as good medical care itself. Whatever criteria we use must constantly be reviewed and rigorously judged from the standpoint of their effects on the patient rather than on the education or convenience of the physician.

Good medical care, even in a scientific age, must still depend on the dedicated and well-trained physician. If we cultivate this attitude and create an environment in which it is commonplace, our medical students should learn that a good medical history is characterized as much by detailed knowledge of the personality of the patient as by an accurate analysis of the physical manifestations of his disease. With interest focused on the individual person, our goals must still be health and happiness. Each member of our house staff must still keep one thought uppermost as he approaches each new patient: How can I help this patient, and as I do so, what can I learn?

32 Fruit St. (14).

DIAGNOSIS OF LEFT-SIDED SUBPHRENIC ABSCESS

Capt. Martin C. Rosner
and
Capt. Morton A. Bosniak, (MC), U. S. A. F.

A patient who had undergone two laparotomies progressed well until the 11th day after the second operation; removal of a drain on that day was followed by fever, pain, and other symptoms suggesting the presence of an abscess. The location of the abscess under the left hemidiaphragm was revealed by roentgenography after the stomach had been moderately distended by having the patient drink a carbonated beverage. The abscess was then drained at a third laparotomy. All infection was cleared by therapy with chloramphenicol, and the patient recovered. Filling the stomach with air and carbon dioxide has certain advantages over filling with barium sulfate. In this case the altered contour of the stomach settled the diagnosis, and the same technique made it possible to follow the recovery process.

Prior to the advent of chemotherapy and antibiotics the diagnosis of subphrenic abscess was indeed a grim one, and all too often made only at autopsy. Ochsner and De Bakey[1] reported 985 deaths in 1,096 patients (89.8%) not subjected to operation, whereas there were 637 deaths among 1,492 patients (32.8%) in whom operation was performed. Numerous authors have emphasized the even graver difficulties associated with left-sided subphrenic abscess. Although roughly 25% of subphrenic abscesses are on the left side, clinicians have been inclined to disregard this variety and discard the diagnosis of subdiaphragmatic suppuration when a right-sided subphrenic abscess has been excluded. Because of the mobility of the structures situated beneath the left side of the diaphragm the characteristic clinical signs may be difficult to elucidate. Yet this very feature promotes a burrowing, multiloculated kind of abscess, with a tendency to rupture into the thorax or abdominal viscera, accounting for the higher over-all mortality in the left-sided as opposed to the right-sided lesions; thus Neuhof and Schlossmann[2] cited a 75% mortality in the former contrasted with 35% in the latter.

Since the inception of antibiotic therapy survey of the literature reveals a striking paucity of commentary on subphrenic abscess; but Rabin,[3] writing in 1951, stated, "The use of chemotherapy and antibiotics in recent years has diminished the number of cases of subphrenic abscess, but the mortality generally still remains high and the course after drainage, prolonged. . . . Although these drugs have diminished the number of cases of subphrenic abscess, they have also increased the number in which the onset is insidious."

The purpose of this paper is to present a typical case of left-sided subphrenic abscess, with a brief review of the diagnostic criteria, clinical and roentgenographic, and a suggested modification in roentgenologic technique which may aid in the diagnosis; it is hoped thereby to call fresh attention to a serious condition, which, although less frequently encountered than in the past, may be all the more difficult to diagnose.

Report of a Case

A 37-year-old staff sergeant was admitted for the second time to the 7510th U. S. A. F. Hospital on Sept. 2, 1958, with epigastric pain and tenderness relieved by alkali or food. A duodenal ulcer had been demonstrated roentgenographically in 1954 and again in December, 1957. The patient had undergone periods of intensive therapy with proper diet and antacid and antispasmodic medication, but his symptoms recurred, persisted, and increased up to the time of the present admission. There was no history of significant disease, and admission physical examination of this tall, asthenic man was unrevealing except for mild epigastric tenderness; results of blood cell count, fasting blood sugar and blood urea nitrogen level determinations, urinalysis, chest x-ray, and electrocardiogram were within normal limits. A final trial of medical therapy was unsuccessful in completely relieving his pain, and a gastrointestinal series revealed the suspected posterior penetrating duodenal ulcer. He was transferred to the surgical service and subjected to a 70% gastric resection on Sept. 25. On Oct. 4 the patient developed cramping epigastric pain and vomiting with the roentgenographic picture of mechanical obstruction of the small intestine; after intubation failed to relieve the obstruction, laparotomy was performed with lysis of adhesions. Postoperatively the patient was placed on therapy with 600,000 units of procaine penicillin and 0.5

Assistant Chief, Medical Service (Captain Rosner), and Chief, Radiology Service (Captain Bosniak), 7510th U. S. A. F. Hospital. Captain Bosniak is now at the Department of Radiology, New York Hospital–Cornell Medical Center, New York.

Gm. of streptomycin twice a day, and he remained afebrile and progressed satisfactorily. The antibiotic therapy was discontinued after four days.

On Oct. 15, the day the drain was removed from the left upper quadrant stab wound, he began to exhibit a spiking temperature with peaks of 102 F (38.9 C). The fever was accompanied by headache, anorexia, left posterior thoracic discomfort, and left shoulder pain. Drainage of a small stitch abscess revealed Aerobacter aerogenes on culture. Three blood cultures were sterile; throat and sputum cultures contained no pathogens; and a urine culture grew out Proteus vulgaris, although the urinalysis showed neither pyuria nor albuminuria. A chest x-ray (fig. 1) showed fluid at the left lung base, although the possibility of underlying parenchymal disease could not be excluded. He was treated with oxytetracycline (Terramycin), 1 Gm. per day for four days, for possible pneumonia, but without improvement.

A medical consultation was requested on Oct. 18. A thoracentesis performed then was productive of 750 cc. of clear yellow fluid, with the characteristics of a transudate. In addition, the patient had moderate left upper quadrant tenderness and guarding, and a small amount of purulence was observed at the former drainage site. A post-thoracentesis x-ray showed elevation of the left hemidiaphragm, which had a somewhat ragged contour, absence of parenchymal lung disease, and disk atelectasis at the left base. It was felt that a left subphrenic collection or abscess was likely, and roentgenologic consultation was requested. Fluoroscopy disclosed an immobile, elevated left hemidiaphragm. Air was introduced into the stomach by the administration of a carbonated beverage and an impression was noted on the superior lateral aspect of the stomach bubble, along with medial and inferior displacement of the stomach remnant by a subphrenic mass (fig. 2).

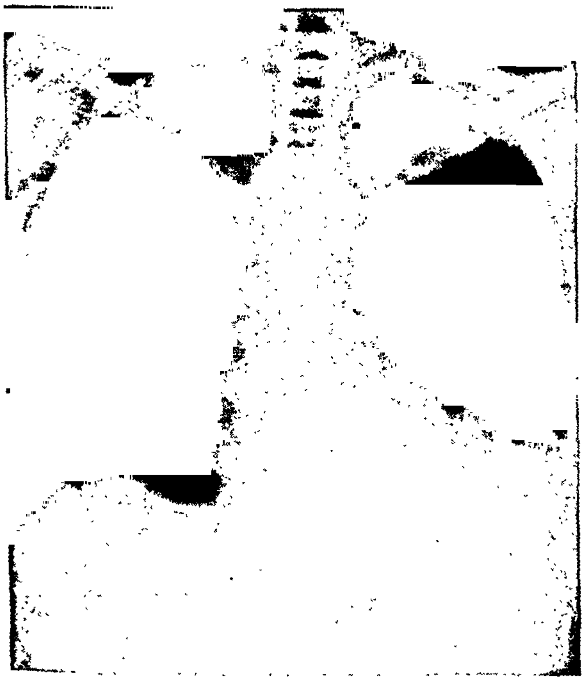

Fig. 1.—Initial roentgenogram of chest, showing pleural effusion at left base somewhat obscuring elevated left hemidiaphragm.

It was decided to institute intensive antibiotic therapy, and the patient was treated with 20 million units of penicillin intravenously during each 24-hour period and 0.5 Gm. of streptomycin intramuscularly twice a day. By Oct. 20, two days after the commencement of the intensive antibiotic therapy, the patient had become afebrile and asymptomatic except for minimal, left-sided, posterior thoracic discomfort and mild left upper quadrant tenderness. When the patient's temperature rose to 101 F (38.3 C) on Oct. 24, with concomitant increase in left upper quadrant tenderness, laparotomy was performed, with drainage of a left subphrenic abscess. Culture of the pus revealed hemolytic Staphylococcus aureus initially sensitive to all antibiotics, but a second culture and sensitivity test of the drainage on Oct. 28 revealed the organism to be insensitive to all antibiotics except chloramphenicol and erythromycin. He was treated with the former drug and made an uneventful recovery. Repeat examination of the stomach remnant on Jan. 12, with use of the same radiologic techniques as were previously used to demonstrate the abscess, showed complete resolution of the previously described changes (fig. 3).

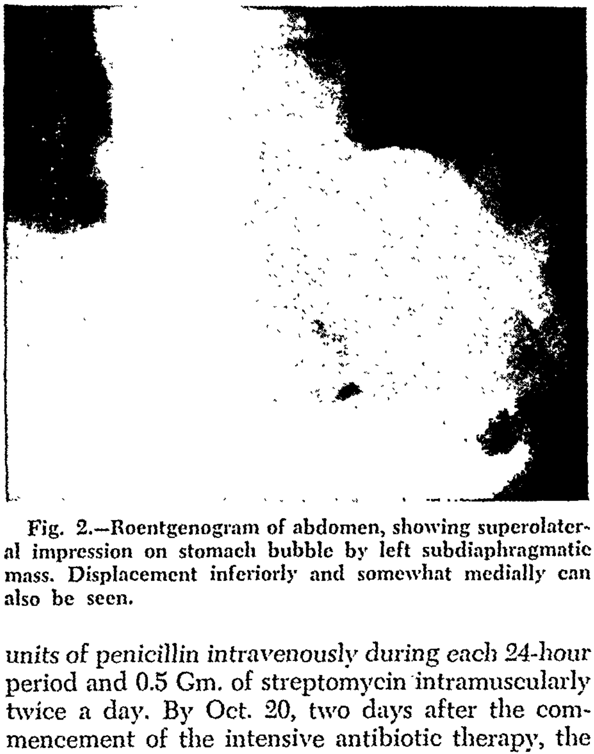

Fig. 2.—Roentgenogram of abdomen, showing superolateral impression on stomach bubble by left subdiaphragmatic mass. Displacement inferiorly and somewhat medially can also be seen.

Clinical and Diagnostic Picture

Although left-sided subphrenic abscesses due to suppuration in the left lung base and even the pelvis have been reported, the most frequent clinical picture is one of prior upper abdominal surgery with lesions of the stomach, duodenum, and occasionally biliary tree predominating.[4] In a small number of cases there may be a relatively acute onset of symptoms 10 days to three weeks after surgery, but in most the onset is so insidious that the diagnosis may not be suspected for many weeks or months.[2]

Usually, but not invariably, fever and leukocytosis are present, along with signs of generalized toxicity such as chills, diaphoresis, anorexia, weakness, malaise, and weight loss. This is perhaps the signal for the clinician to recall Carter's modification of the old adage: "Pus somewhere, pus nowhere, pus not under the right diaphragm, pus under the left diaphragm." [5]

A variety of signs and symptoms referable to the thorax, the abdomen, or both may be present. Cough may occur, due to compression or basal collapse of the lung, and hiccough, due to diaphragmatic irritation.[6] Pain in the lower part of the chest and along the costal margin is often manifest, while authors differ markedly concerning the frequency of pain referred to the left shoulder and neck.[7] Abdominal pain and gastrointestinal symptoms such as vomiting, although frequent, are less common. A valuable clue is a local fulness of the chest, with a loss of elasticity of the chest wall and obliteration of the intercostal spaces. Of importance among the early findings is a point of tenderness on the chest wall where the abscess is most superficial, or, quite as significant but more often overlooked, an area of localized edema; either may not only reveal the diagnosis but provide the best localizing sign short of actual pus on aspiration.[3] Upper abdominal tenderness is a less useful sign, particularly soon after a gastrectomy.

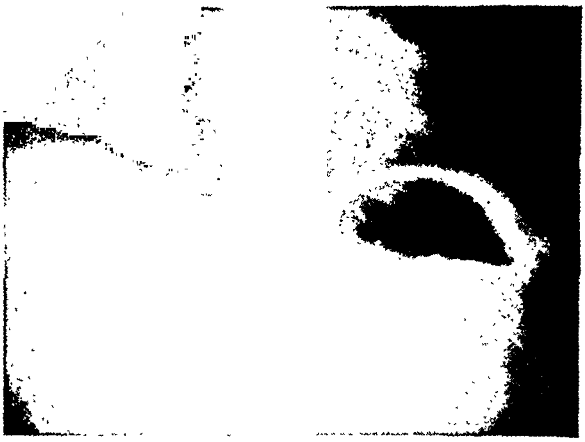

Fig. 3.—Roentgenogram taken three months after operation. Stomach bubble is in normal anatomic position.

Of vital significance is the presence of pleural effusion over the left diaphragm, and, less provocative, basilar atelectasis.[5] Neuhof and Schlossmann [2] reported "a pleural or pulmonopleural inflammatory process" in 78% of their cases, and a thoracoabdominal complex of signs in 31%. The discovery of a pleural effusion after abdominal surgery should immediately alert the clinician to the likelihood of a subphrenic abscess. A grievously frequent error has been to attribute such a sympathetic effusion to postoperative pneumonia, which rarely causes a pleural effusion and is almost inevitably accompanied by abundant sputum production from a purulent bronchitis. Before antibiotics the clear sympathetic effusion would become an infected empyema, but today the fluid remains clear, except in neglected cases; but a subphrenic abscess should at least be suspected in any empyema which does not clearly originate in the lung.[1]

A difference of opinion exists as to the advisability of exploratory aspiration for pus by introducing a needle through the diaphragm. In Neuhof and Schlossmann's series [2] pus was obtained by this means in 14 of 17 puzzling cases, and they strongly endorsed this procedure, with the needle left in situ as a guide to operation; they cautioned against false security derived from a negative result of aspiration, since the needle may be too short to reach a mediosplenic abscess under the central point of the diaphragm. Others, including Ochsner and De Bakey,[1] Rabin,[3] and Harley,[8] interdict this procedure, warning of the possibilities of perforation of a viscus or pleural contamination. Rabin [3] further advised care in decisions concerning the origin of pus aspirated through the seventh or eighth interspace, since infrapulmonary empyema is easily confused with a subphrenic abscess. He stressed the importance of a recent tooth extraction or unconsciousness in the differential diagnosis, attributing most infrapulmonary empyemas to perforated lung abscesses.

To further confuse the clinical picture Hochberg[9] emphasized that 5% of his 139 cases had fever, chills, and costovertebral angle pain and tenderness, and Beach and Tynan [6a] were concerned about the occasional difficulty of differentiation between a perinephric abscess and a subphrenic abscess with concomitant perinephritis. Of paramount importance, then, is the radiologic evidence.

Roentgenologic Aspects

The roentgenologic changes generally encountered in cases of subdiaphragmatic abscess have been described in many exhaustive and extensive reports on this subject. The case presented here offers an opportunity to review these changes as well as to describe a modification of technique in the study and detection of left-sided subphrenic abscess. Adequate roentgenologic examination, of course, is necessary in any suspected case of subphrenic disease, but the types of study and the findings will vary with the side of involvement and the extent of this involvement. Because of the difference of the anatomy of the right and left subphrenic spaces the roentgenologic findings in disease of these areas will differ. On the right the space and the spread of an abscess is limited inferiorly by the liver. Therefore, manifestation of disease on this side will affect the right diaphragm and the thorax more readily than will disease on the left, where the space is bounded inferiorly by the spleen, stomach, colon, and left lobe of liver—organs that can easily be displaced and moved. Consequently, abscess on this side, although it will affect the diaphragm and thorax, will also displace and affect the organs of the left upper quadrant, thereby giving the investigator a further chance to evaluate this area and make the diagnosis.

The routine roentgenogram of the chest frequently gives the first indication of disease under the diaphragm. Pleural effusion, considerable in amount or possibly minimal, occurs in the majority of cases of subphrenic abscess.[10] To detect small pleural effusion a roentgenogram made with the patient in the decubitus position with the involved side down is frequently valuable.

Fixation of the affected diaphragmatic leaflet in an elevated position is the most common and important roentgenologic sign of subphrenic disease.[11] This was found to be present in over 80% of Ochsner and De Bakey's cases. If a lateral film is obtained, localized flattening and elevation of the normal diaphragmatic contour, usually posteriorly, can also be frequently seen.[12] It has been noted that elevation of the diaphragm is more common in right-sided lesions and often not seen in those on the left because of previously mentioned anatomic differences.[13] Fixation of the diaphragm will occur in left-sided lesions, not infrequently, even without elevation.[5] Moreover, Neuhof and Schlossmann [2] state that neither diaphragmatic elevation nor fixation was present in 40% of their series of patients with left-sided subphrenic abscesses, while these diaphragmatic changes are rarely absent on the right.[14]

It must be remembered, however, that while an elevated, fixed diaphragm is characteristic and suggestive of subphrenic disease, other conditions may produce similar findings. For example, the most common and important of these is splinting of the diaphragm with a relative decrease in excursions secondary to recent surgery in the involved area. This is especially true of surgery of the right upper quadrant.[10]

The lung tissue above the elevated diaphragm is somewhat compressed, leading to disk atelectasis, which, when seen, should always suggest disease below the diaphragm. Occasionally, but much more rarely, more extensive atelectasis or even pneumonitis occurs in the basilar segments of the adjacent lung. The extensive roentgenologic changes which are seen with the more severe thoracic complications are beyond the scope of this discussion.[15]

Much has been written on the value of free air, or an air-fluid level, under the affected diaphragm in diagnosing this condition. There is no more definite roentgenologic sign than this when it occurs; however, the frequency reported in the literature varies, the figure most often quoted being about 25%.[16] The incidence appears to be much lower, however, in left-sided abscesses, and it is more likely to be missed on this side because gas from the stomach and colon obscures the area.[3] The air apparently originates from perforation of a viscus and not from anaerobic bacterial growth, as was previously considered. Air may be present under the diaphragm two or three weeks after abdominal surgery, and this must be kept in mind when a diagnosis of subphrenic abscess is made on the basis of this sign.[5]

Left-sided subphrenic abscess can be further delineated by keeping in mind the anatomic relation of the stomach to the subdiaphragmatic space. It has been suggested that when barium is placed in the stomach, displacement by a left subphrenic inflammatory mass can be demonstrated. Carter [5] and Friedman [10] advise that after ingestion of barium the patient be placed in the Trendelenburg position; the fundus of the stomach will normally be against the inferior diaphragmatic surface. However, if an abscess is present the stomach may be displaced inferiorly or possibly medially or anteriorly. Neuhof and Schlossmann [2] describe filling the stomach with air, by means of Seidlitz powder, and thereby visualizing the density of the abscess through the lucency of the gastric air bubble. These authors also described the anterior displacement of the stomach bubble by an abscess mass.

In the present case the patient was given a carbonated beverage to drink, and when he was in the upright position the air bubble was seen to be inferiorly placed; but, more important, an actual impression on the lateral superior aspect of the stomach bubble was produced (fig. 2). A similar study was performed on this patient three months after drainage of a left-sided subphrenic abscess, and the stomach bubble was then seen to be in its normal position with no residual impression (fig. 3). A review of the literature fails to reveal a similar published experience, although controversy exists as to the significance of indentation versus displacement of the barium-filled stomach in left-sided subphrenic masses.[2]

We believe that air is superior to barium as a contrast medium in the stomach in the study of left-sided subphrenic abscess, because it is much lighter than barium and therefore the stomach wall can be indented more easily, allowing a small abscess to be seen more readily. Also, air will expand the fundus of the stomach to a greater extent than barium and therefore has a greater chance of coming in contact with a subphrenic collection. In case of a perforation it is much safer to administer air and fluid than barium. The advantage of using air becomes even more obvious if an intestinal perforation is suspected and the patient is receiving nothing by mouth; the examination for subphrenic abscess can still be performed by passing a nasogastric tube into the stomach and administering approximately 120 cc. of air in this way. After the appropriate films are taken the air can easily be withdrawn.

Finally, other procedures, such as diagnostic pneumoperitoneum and kymography, have been employed but found to be of limited use.

Comment

Probably the most important factor in the diagnosis of left-sided subphrenic abscess is the clinician's readiness to consider the diagnosis. The case reported here illustrates that a left-sided subphrenic abscess could and did develop despite routine postoperative antibiotic therapy, which may actually mask the situation and so demand greater alertness to the possibility on the part of the clinician. A clinical picture consistent with suppuration, within a variable length of time after upper abdominal surgery, should automatically suggest the possibility of a diagnosis of left-sided subphrenic abscess; the presence of a pleural effusion, or, less frequently, a thoracoabdominal complex should spur the clinician to attempt demonstration of the abscess by radiologic techniques. In this regard, it is the belief of the authors that the use of air to inflate the stomach or stomach remnant will greatly assist in delineating the abscess, particularly while it is still small. It is then, when the patient has not yet been debilitated by a lengthy battle against a chronic suppurative process nor as yet suffered a grave complication, such as rupture of the abscess into a viscus or the thorax, that he is more likely to respond to treatment.

The advice of Zaslow and Sachs[17] concerning treatment of the abscess with antibiotics appears judicious. These authors reported the cure of subphrenic abscess with intravenous therapy with oxytetracycline and quoted Maingot's recommendation that conservative treatment be attempted for three to six days, drawing on Crile's[18] extensive experience with penicillin treatment of intraabdominal abscesses. They proposed such therapy only so long as improvement continues and recommended instituting immediate surgical drainage at the cessation of resolution or the first sign of deterioration. In such a case, they believed, intensive antibiotic therapy at least promotes localization of the abscess and makes the patient a better operative risk. Just such a plan was followed in the case reported here, with striking improvement after the administration of massive doses of penicillin intravenously but subsequent deterioration, necessitating surgical drainage.

Concerning the proposal of Beach and Tynan[6a] that the clinician "cling and wait" for the abscess to point, because of possible confusion with a perinephric abscess, perusal of the literature caused us to feel that all too often the abscess might "point" into a viscus or the thorax. If roentgenologic techniques, including the one described in this paper, cannot further illuminate the situation, the exceedingly small number of cases of perinephric abscess that may be confused with subphrenic abscess[2] still do not justify accepting the risk of a perforation imposed by waiting, even with protective antibiotics.

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REEVALUATION OF MODERN ANTIBACTERIAL AGENTS USED FOR PERIRENAL ABSCESS

John J. Murphy, M.D.
and
F. Peter Kohler, M.D., Philadelphia

Diagnostic criteria, clinical course, and therapeutic results in cases of perirenal abscess were studied in 12 patients hospitalized with that diagnosis in the years 1937-1942. The data were compared with those from a similar group of 13 patients hospitalized in the years 1952-1958. The pattern of renal infections has changed in recent years. The later group of patients were older. were less acutely sick on admission, and had to be hospitalized longer. Their course was exemplified by that of a 52-year-old woman with a long history of calculi and other urologic troubles; these had culminated in marked fever and paralytic ileus after a retrograde pyelogram was taken, when contrast medium extravasated into a large perirenal cavity. Recovery followed incision and drainage of the perirenal abscess. The authors consider this the treatment of choice for perirenal abscess and conclude that antibacterial agents are ineffective in chronic parenchymal renal disease.

Infection of the renal parenchyma is the usual cause of perirenal abscess. Rupture of an abscess in the cortex of the kidney into the surrounding fat, with formation of a secondary collection in the space confined by Gerota's fascia, is thought to be the usual course of events. Infection anywhere in the body which causes bacteremia may lead to a cortical renal abscess and eventually to perirenal involvement. Primary infections in certain organs are frequent sources of renal cortical abscesses. Among these are dental and tonsillar abscesses, furuncles of the skin, and acute prostatitis. Within the kidney, pyonephrosis, nephrolithiasis, post-traumatic infection, and renal tuberculosis are common causes. Before the era of modern antibacterial agents, hemolytic Staphylococcus aureus was the offending organism in 80% of reported cases. Other organisms cultured were hemolytic streptococcus, Escherichia coli, Pseudomonas, Aerobacter aerogenes, and Proteus.

Reviews on perirenal abscess by Nesbit and Dick,[1] Hammer,[2] Campbell,[3] and Atcheson[4] stress the severely febrile course of the patient prior to drainage, with chills, marked tenderness and pain in the affected flank, and the usual absence or paucity of urinary symptoms or findings. Nesbit emphasizes that routine urine examinations may show completely normal findings in the presence of staphylococcic urinary tract infections and that staining of the urinary sediment is necessary to reveal the presence of the bacteria. The illnesses reviewed were usually of short duration and accompanied by a marked leukocytosis and slight anemia.

Aids in the diagnosis of perirenal abscess have been described by Beer[5] and Lipsett,[6] who emphasized characteristic roentgenographic findings such as absence of the psoas shadow on the affected side and elevation of the diaphragm. Others describe fixation of the kidney[7] and scoliosis of the vertebral column with the concavity of the curvature toward the involved side.[8] Retrograde pyelograms may indicate the presence of a perirenal abscess by demonstrating contrast medium in the perirenal space which communicates with the renal pelvis.[9]

Prior to the advent of effective antibacterial therapy, patients who developed a perirenal abscess were treated by incision and drainage as soon as the diagnosis was made. The literature preceding the development of modern antibacterial agents stresses the importance of early diagnosis of this condition and the necessity for immediate drainage in order to effect a cure and avoid complications. Failure to drain the abscess early often results in spread of infection to neighboring tissues. Nesbit and Dick[1] reported 16.5% pulmonary complications in 85 perirenal abscesses with six perinephrobronchial fistulas. Kuester[10] reported that 34 of 230 abscesses ruptured into the peritoneal cavity. Often the purulent material dissects along the psoas muscle of the involved side to point in the inguinal canal.

Incision and drainage of the abscess was acknowledged to be the proper therapy, and Campbell[3] states that a patient rarely recovered without operation. Even with drainage, the mortality was 24.5%, according to Hunt,[11] with 6.6% of deaths occurring immediately postoperatively and 17.9% within five years after operation.

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Department of Surgery, Division of Urology of the Hospital of the University of Pennsylvania.

becomes even more obvious if an intestinal perforation is suspected and the patient is receiving nothing by mouth; the examination for subphrenic abscess can still be performed by passing a nasogastric tube into the stomach and administering approximately 120 cc. of air in this way. After the appropriate films are taken the air can easily be withdrawn.

Finally, other procedures, such as diagnostic pneumoperitoneum and kymography, have been employed but found to be of limited use.

Comment

Probably the most important factor in the diagnosis of left-sided subphrenic abscess is the clinician's readiness to consider the diagnosis. The case reported here illustrates that a left-sided subphrenic abscess could and did develop despite routine postoperative antibiotic therapy, which may actually mask the situation and so demand greater alertness to the possibility on the part of the clinician. A clinical picture consistent with suppuration, within a variable length of time after upper abdominal surgery, should automatically suggest the possibility of a diagnosis of left-sided subphrenic abscess; the presence of a pleural effusion, or, less frequently, a thoracoabdominal complex should spur the clinician to attempt demonstration of the abscess by radiologic techniques. In this regard, it is the belief of the authors that the use of air to inflate the stomach or stomach remnant will greatly assist in delineating the abscess, particularly while it is still small. It is then, when the patient has not yet been debilitated by a lengthy battle against a chronic suppurative process nor as yet suffered a grave complication, such as rupture of the abscess into a viscus or the thorax, that he is more likely to respond to treatment.

The advice of Zaslow and Sachs[17] concerning treatment of the abscess with antibiotics appears judicious. These authors reported the cure of subphrenic abscess with intravenous therapy with oxytetracycline and quoted Maingot's recommendation that conservative treatment be attempted for three to six days, drawing on Crile's[18] extensive experience with penicillin treatment of intraabdominal abscesses. They proposed such therapy only so long as improvement continues and recommended instituting immediate surgical drainage at the cessation of resolution or the first sign of deterioration. In such a case, they believed, intensive antibiotic therapy at least promotes localization of the abscess and makes the patient a better operative risk. Just such a plan was followed in the case reported here, with striking improvement after the administration of massive doses of penicillin intravenously but subsequent deterioration, necessitating surgical drainage.

Concerning the proposal of Beach and Tynan[6a] that the clinician "cling and wait" for the abscess to point, because of possible confusion with a perinephric abscess, perusal of the literature caused us to feel that all too often the abscess might "point" into a viscus or the thorax. If roentgenologic techniques, including the one described in this paper, cannot further illuminate the situation, the exceedingly small number of cases of perinephric abscess that may be confused with subphrenic abscess[2] still do not justify accepting the risk of a perforation imposed by waiting, even with protective antibiotics.

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REEVALUATION OF MODERN ANTIBACTERIAL AGENTS USED FOR PERIRENAL ABSCESS

John J. Murphy, M.D.
and
F. Peter Kohler, M.D., Philadelphia

Diagnostic criteria, clinical course, and therapeutic results in cases of perirenal abscess were studied in 12 patients hospitalized with that diagnosis in the years 1937-1942. The data were compared with those from a similar group of 13 patients hospitalized in the years 1952-1958. The pattern of renal infections has changed in recent years. The later group of patients were older. were less acutely sick on admission, and had to be hospitalized longer. Their course was exemplified by that of a 52-year-old woman with a long history of calculi and other urologic troubles; these had culminated in marked fever and paralytic ileus after a retrograde pyelogram was taken, when contrast medium extravasated into a large perirenal cavity. Recovery followed incision and drainage of the perirenal abscess. The authors consider this the treatment of choice for perirenal abscess and conclude that antibacterial agents are ineffective in chronic parenchymal renal disease.

Infection of the renal parenchyma is the usual cause of perirenal abscess. Rupture of an abscess in the cortex of the kidney into the surrounding fat, with formation of a secondary collection in the space confined by Gerota's fascia, is thought to be the usual course of events. Infection anywhere in the body which causes bacteremia may lead to a cortical renal abscess and eventually to perirenal involvement. Primary infections in certain organs are frequent sources of renal cortical abscesses. Among these are dental and tonsillar abscesses, furuncles of the skin, and acute prostatitis. Within the kidney, pyonephrosis, nephrolithiasis, posttraumatic infection, and renal tuberculosis are common causes. Before the era of modern antibacterial agents, hemolytic Staphylococcus aureus was the offending organism in 80% of reported cases. Other organisms cultured were hemolytic streptococcus, Escherichia coli, Pseudomonas, Aerobacter aerogenes, and Proteus.

Reviews on perirenal abscess by Nesbit and Dick,[1] Hammer,[2] Campbell,[3] and Atcheson[4] stress the severely febrile course of the patient prior to drainage, with chills, marked tenderness and pain in the affected flank, and the usual absence or paucity of urinary symptoms or findings. Nesbit emphasizes that routine urine examinations may show completely normal findings in the presence of staphylococcic urinary tract infections and that staining of the urinary sediment is necessary to reveal the presence of the bacteria. The illnesses reviewed were usually of short duration and accompanied by a marked leukocytosis and slight anemia.

Aids in the diagnosis of perirenal abscess have been described by Beer[5] and Lipsett,[6] who emphasized characteristic roentgenographic findings such as absence of the psoas shadow on the affected side and elevation of the diaphragm. Others describe fixation of the kidney[7] and scoliosis of the vertebral column with the concavity of the curvature toward the involved side.[8] Retrograde pyelograms may indicate the presence of a perirenal abscess by demonstrating contrast medium in the perirenal space which communicates with the renal pelvis.[9]

Prior to the advent of effective antibacterial therapy, patients who developed a perirenal abscess were treated by incision and drainage as soon as the diagnosis was made. The literature preceding the development of modern antibacterial agents stresses the importance of early diagnosis of this condition and the necessity for immediate drainage in order to effect a cure and avoid complications. Failure to drain the abscess early often results in spread of infection to neighboring tissues. Nesbit and Dick[1] reported 16.5% pulmonary complications in 85 perirenal abscesses with six perinephrobronchial fistulas. Kuester[10] reported that 34 of 230 abscesses ruptured into the peritoneal cavity. Often the purulent material dissects along the psoas muscle of the involved side to point in the inguinal canal.

Incision and drainage of the abscess was acknowledged to be the proper therapy, and Campbell[3] states that a patient rarely recovered without operation. Even with drainage, the mortality was 24.5%, according to Hunt,[11] with 6.6% of deaths occurring immediately postoperatively and 17.9% within five years after operation.

From the Harrison Department of Surgical Research, Schools of Medicine, University of Pennsylvania, and the Department of Surgery, Division of Urology of the Hospital of the University of Pennsylvania.

The addition of potent antibacterial agents to the physician's armamentarium was accompanied by excessive optimism regarding the eradication of this bacterial infection. Occasional enthusiastic *reports*[12] *appeared in the literature about the suc*cessful treatment of renal carbuncles and renal cortical abscesses by means of these agents. It soon became evident[13] that the antibacterial drugs did not always eradicate the infection but often masked the true signs and symptoms of the disease process.

Recently, within a short time interval, several gravely ill patients with perirenal abscesses were admitted to the University Hospital. These persons had been treated with antibacterial agents for a long time, with suppression of their acute septic episodes in part but with gradual decline of their general physical condition. In each patient, drainage of the collection of purulent material resulted in a restoration of general well-being and health.

TABLE 1.—*Salient Features of Twelve Patients with Perirenal Abscess*

Patient No.	Age, Yr.	Sex	Length of Illness Prior to Admission	Temperature at Admission, F	Hemoglobin Level, % of Normal*	White Blood Cell Count at Admission, per Cu. Mm.	Blood Urea Nitrogen Level, Mg.%	Organism in Abscess	Organism in Urine
1†	37	F	2 wk.‡	103.0	60	13,000	60	Aerobacter	Aerobacter
2	19	M	2 wk.§	102.0	74	27,600	9	Hemolytic Staph. aureus	....
3	27	M	2 wk.‖	102.8	37	21,000	16	Hemolytic streptococcus	Proteus
4	28	F	1 mo.	101.8	73	17,900	11	Nonhemolytic Staph. aureus, Esch. coli, Aerobacter	....
5	29	M	2 da.	103.0	92	19,700	15	Proteus	Proteus
6	34	F	6 hr.	105.0	70	11,000	10	Esch. coli	Esch. coli
7	24	M	5 da.	103.0	60	16,000	19	Hemolytic Staph. aureus	Hemolytic Staph. aureus
8	22	M	6 wk.	104.0	79	26,700	15	Hemolytic Staph. aureus	None
9	32	M	4 wk.	103.0	80	18,000	15	Hemolytic Staph. aureus	Hemolytic Staph. aureus, Esch. coli
10	44	M	10 da.	102.0	60	28,000	54	Nonhemolytic Staph. aureus	Nonhemolytic Staph. aureus
11	22	M	3 wk.	102.0	70	18,000	15	Hemolytic Staph. aureus	....
12	39	M	2 wk.	102.0	43	11,800	23	Hemolytic Staph. aureus, Esch. coli	Esch. coli
Av.	29	..	2.3 wk.	102.8	66	19,060	22	....	....

* Normal = 14 Gm.%.
† Died.
‡ Tooth extraction, backache.
§ Pain in upper right quadrant.
‖ Pain in left flank.

TABLE 2.—*Characteristics of Disease in*

Patient No.	Age, Yr.	Sex	Length of Illness Prior to Admission	Temperature at Admission, F	Hemoglobin Level, Gm.%	White Blood Cell Count at Admission, per Cu. Mm.	Blood Urea Nitrogen Level, Mg.%	Organism in Abscess	Organism In Urine
13	45	F	2 mo.	100.4	10.5	12,400	15	Aerobacter, Pseudomonas	Aerobacter, Pseudomonas
14	51	F	8 wk.	101.0	4.2	14,300	12	Aerobacter	Aerobacter
15	35	M	6 wk.	100.0	5.6	14,000	49	Proteus, Aerobacter	Proteus
16	46	F	1 wk.	104.0	11.26	26,800	32	Esch. coli Pseudomonas, Proteus	Proteus
17	45	F	3 wk.	99.0	9.5	14,900	29	Paracolon, Proteus	Proteus
18	7	F	10 da.	101.0	8.7	8,900	21	Proteus, Esch. coli	Proteus
19*	26	F	6 mo.	102.0	5.4	22,300	86	Proteus, Esch. coli	Proteus
20	65	M	3 wk.	100.0	14.1	7,700	14	Proteus	Proteus
21	65	M	5 mo.	99.0	10.7	10,300	16	Nonhemolytic streptoccus, 7,300 cc. fluid in abscess cavity	No growth
22	58	M	9 wk.	98.0	7.4	9,800	33	Esch. coli, 600 cc. fluid in abscess cavity	No growth
23	53	F	2 mo.	100.8	6.1	9,200	14	Proteus, 700 cc. in abscess cavity	Proteus
24	52	F	7 mo.	100.8	7.4	6,000	43	Aerobacter, 3,000 cc. fluid in abscess cavity	Pseudomonas
25	60	M	1 yr.	99.4	5.9	5,000	22	Proteus, 300 cc. fluid in abscess cavity	Proteus
Av.	47	..	13 wk.	100.5	8.2	12,400	30		

* Died.

In order to determine the effect of modern antibacterial therapy on the treatment of perirenal abscesses, a survey was made of the experience with this lesion in the University Hospital in the era preceding the antibacterial agents and in a recent similar period of time. Table 1 lists the salient features of 12 patients admitted to the University Hospital with a diagnosis of perirenal abscess between July, 1937, and October, 1942.

Related Infection	Lithiasis	Admission Date	Discharge Date
Pelvic inflammatory disease, chronic pyelonephritis	None	7/26/37	8/21/37
Sinusitis since 1935	None	12/21/37	1/21/38
Periurethral abscess, stricture for 5 mo.	None	12/23/37	1/30/38
....	Ureteral stone	1/23/38	2/ 4/38
Pyelolithotomy June, 1939	Previous renal calculus	8/12/39	8/31/39
Urinary tract, 4 yr.	Renal calculus on right, 4 yr.	5/ 6/39	6/27/39
Urinary tract	Pyelolithotomy on right, calculus	8/18/40	8/29/40
Sore throat	....	12/ 4/39	1/ 1/40
....	....	4/21/41	5/19/41
Urinary tract	Bilateral calculus since 1933	1/14/42	3/28/42
Upper respiratory tract	None	5/ 9/42	6/ 8/42
Pyelolithiasis, 13 yr. ago	Bilateral renal calculus	10/31/42	11/29/42
....	....	....	....

Most of these patients were in the second and third decade of life and were admitted to the hospital with a relatively short history of illness and with a high fever. Leukocytosis was marked and anemia rare. In 8 of the 12 patients the offending organism was a hemolytic Staphylococcus aureus. Fifty per cent of the patients had concomitant renal calculi or other urinary tract disease. Eleven patients recovered after incision and drainage of the abscess.

Table 2 demonstrates some significant changes in the disease picture as demonstrated by 13 patients admitted to the University Hospital with the diagnosis of perirenal abscess between August, 1952, and October, 1958. These patients were older, the average age being 47 years. The majority had renal calculi and all had a history of urinary tract infection without a history of a distant focus of infection. This may indicate that the antibacterial agents are effective in preventing the spread of bacteria from infections such as sinusitis and tonsillitis to the kidney parenchyma. It would also appear that, in cases of long-standing renal infections, especially when calculi are present, the antibacterial agents are ineffective in preventing spread of the abscess and in reaching and eradicating the central focus. Most of the patients had low-grade fever, and some were afebrile at the time of admission. Leukocytosis was not as marked as in the patients listed in table 1, and moderate to severe anemia was usually found. All had been ill for long periods of time, the shortest period being one week and the longest one year, with an average duration of illness of 13 weeks prior to admission. Staphylococci were only occasionally encountered, whereas Proteus and coliform organisms seemed to predominate. Despite the fact that almost all of the patients had been given two or more supposedly potent antibacterial agents, the infections persisted and produced weight loss, cachexia, and anemia.

The course of one of the patients in the most recent series was thought to merit a detailed description because it clearly demonstrates the extent to which antibacterial agents may mask the clinical picture and hinder a patient's recovery from what should be an acute and brief illness.

Thirteen Patients with Perirenal Abscess

Related Infection	Lithiasis	Antibiotic Given	Admission Date	Discharge Date
Nephrolithotomy on right in 1950, on left in 1949	Bilateral	Penicillin, 300,000 units b.i.d.; sulfadiazine, 0.5 Gm. q.i.d.; streptomycin, 0.5 Gm. q.i.d.; 1 mo.	8/13/52	8/27/52
Nephrolithotomy, 1950	Bilateral	Penicillin, 300,000 units t.i.d.; streptomycin, 0.5 Gm. b.i.d.; 6 wk.	3/16/52	3/16/52
Urinary tract	Bilateral	Penicillin, 300,000 units t.i.d.; sulfadiazine, 0.5 Gm. q.i.d.	7/26/54	8/21/54
Urinary tract	Bilateral	Penicillin, 300,000 units, q.i.d., 3 days	12/29/54	1/23/55
Urinary tract	Bilateral	Chloramphenicol, 250 Gm. q.i.d., 3 wk.	2/24/55	3/ 5/55
Urinary tract	Bilateral	Penicillin; streptomycin; sulfisoxazole; and chloramphenicol; since 1948	9/10/55	9/10/55
Chronic pyelonephritis	None	....	10/ 2/55	10/ 2/55
Chronic pyelonephritis	Pyelolithotomy 1944, calculus 1955	Chloramphenicol, 250 Gm. q.i.d., 1 wk.	2/ 2/58	2/11/58
Urinary tract	Right renal pelvis since age 18	Penicillin; streptomycin; 5 mo.	7/15/58	8/ 4/58
Urinary tract	Bilateral since 1956	Penicillin; chloramphenicol; sulfisoxazole; 9 wk.	9/16/58	10/ 5/58
Urinary tract	Right renal & ureteral calculus	Chloramphenicol, 250 Gm. q.i.d.; nitrofurantoin, 100 Gm. q.i.d., 2 mo.	9/29/58	10/22/58
Urinary tract	Right renal calculus	Chloramphenicol, 10 wk.; polymyxin; kanamycin	10/23/58	11/15/58
Chronic pyelonephritis	None	Chloramphenicol; nitrofurantoin; sulfisoxazole; 3 mo.	10/30/58	12/ 9/58

Report of a Case

A 52-year-old female had an attack of renal colic in 1947. At that time, she passed a calculus, presumably from the right upper part of the urinary tract. An intravenous urogram after the attack was reported to be normal. In 1950, she had another attack of pain in the right flank and hematuria and again passed several calculi. She remained asymptomatic until January, 1958, when she was treated for anorexia, fatigue, and weight loss. She had pyuria but no other definitive symptoms until Feb. 14, when she had an episode of hematuria.

An intravenous pyelogram at that time revealed poor function on the right side, and a retrograde pyelogram on Feb. 18 (fig. 1 and 2) revealed extravasation of the contrast medium from the upper calyx into an irregular cavity which appeared to extend beyond the parenchymal shadow. Two small calculi were seen on the right below the diaphragm in close proximity to this cavity. After the retrograde pyelogram had been made, the patient became extremely ill with marked fever and a paralytic ileus. The blood urea nitrogen level rose to 52 mg.%. Aerobacter aerogenes was found in the urine culture. The patient was treated with chloramphenicol and prednisone (Meticorten) and general supportive therapy. She slowly recovered and was discharged from the hospital on March 30, 1958. Therapy with antibiotics was continued, but her symptoms of anorexia, weight loss, and fatigue persisted and she had to be readmitted July 18, 1958. Early in September, 1958, the antibacterial therapy was discontinued and the patient immediately experienced febrile episodes with a temperature of 102 F (38.9 C) every evening. She also developed gradually increasing pain in the right flank and was readmitted to the hospital on Oct. 10, 1958, with nausea, vomiting, and diarrhea. Chills and fever persisted despite administration of antibacterial agents, and she was transferred to the University Hospital on Oct. 23.

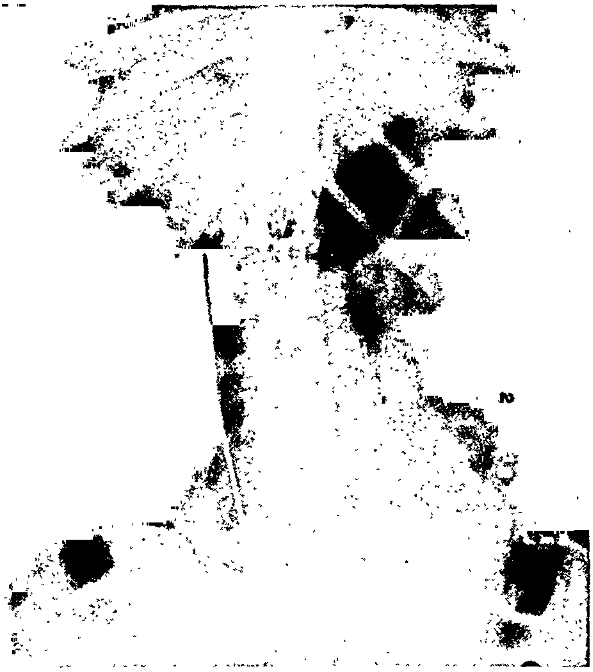

Fig. 1.—Ureteral catheter shown in place. Two calculi are seen within right renal shadow. Note normal right psoas shadow.

At the time of admission, the patient had constant pain in the right flank. She had lost 40 lb. (18 kg.) in the four months preceding admission and was in a state of extreme weakness and exhaustion. There was bilateral pitting ankle edema. She had some dyspnea, and a temperature of 100 F (37.8 C) each evening. At the time of her admission, the blood pressure was 96/66 mm. Hg and the pulse 108 per minute. She was pale and weak. A large fixed and tender mass filled the right side of the abdomen. A roentgenogram of the chest revealed a markedly elevated right side of the diaphragm (fig. 3). Despite supportive therapy, the patient's general condition was slow to improve and the blood urea nitrogen level increased daily. It was felt that the expanding abscess was interfering with drainage from the right kidney. The hemoglobin level was 7.4 Gm.%; the white blood cell count was 6,000 per cubic millimeter, with 72% neutrophils, 24% lymphocytes, and 4% eosinophils. The blood urea nitrogen level was 43 mg.%. Urinalysis revealed a specific gravity of 1.010, 2+ protein, and no sugar. The specimen was loaded with white blood cells and bacteria. Urine culture revealed Pseudomonas. The patient was given a transfusion with whole blood until the hemoglobin level was 12 Gm.%.

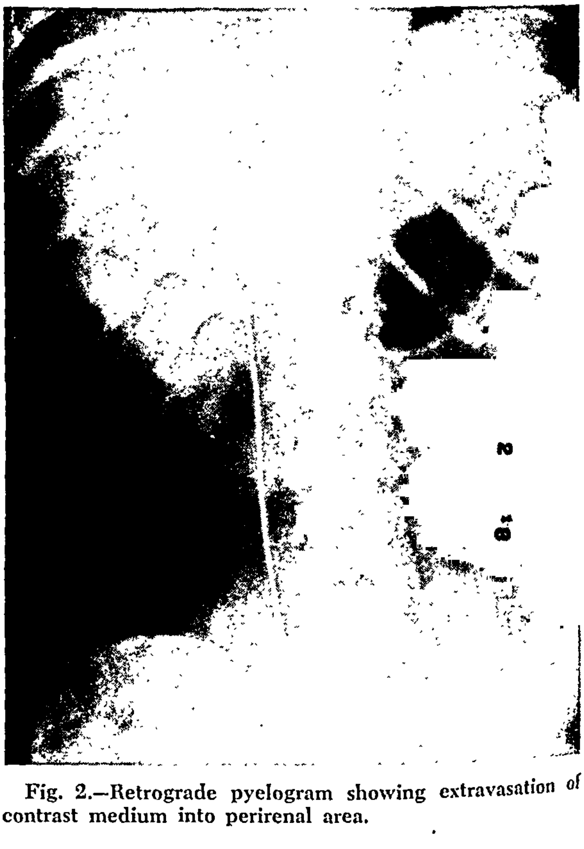

Fig. 2.—Retrograde pyelogram showing extravasation of contrast medium into perirenal area.

Incision and drainage of the abscess in the right retroperitoneal space was carried out on Nov. 4.

Three thousand cubic centimeters of thick white pus was removed and the cavity drained. Aerobacter aerogenes was isolated from the purulent material. The postoperative course was marked by constant improvement in the patient's appearance and strength. She was discharged on Nov. 15.

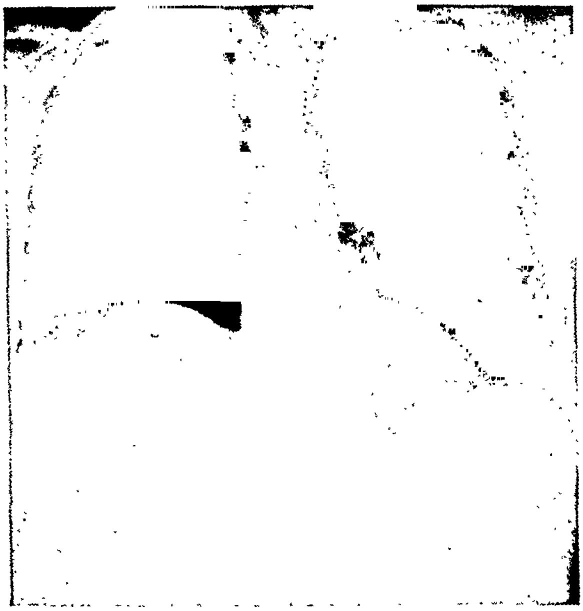

Fig. 3.—Roentgenogram showing elevation of right side of diaphragm.

Summary and Conclusions

The clinical course of patients with perirenal abscess treated before and after the advent of modern antibacterial agents has been compared. It appears likely that these agents have controlled some of the more common sources of renal infection, such as tonsillitis and furunculosis, since the patients in the more recent series were older and almost invariably had serious intrarenal disease. At the same time, it is apparent that the antibacterial agents are ineffective in eradicating chronic parenchymal renal disease. This treatment may mask the symptoms produced by perirenal abscess so that the correct diagnosis is not made. Extreme clinical deterioration of the patient may result. It is apparent that incision and drainage remains the treatment of choice in this disease process.

3400 Spruce St. (4) (Dr. Murphy).

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THYROIDITIS.—The two types of thyroiditis most frequently encountered are subacute thyroiditis and Hashimoto's disease. Subacute thyroiditis is a self-limited disease of unknown etiology, characterized by a tender gland with a diminished I^{131} uptake in the acute phase. Although there is no cure, adrenal steroids and x-ray treatment offer good symptomatic relief. Hashimoto's disease is a distinct and increasingly common clinical entity which must be differentiated from other types of nodular goiter. This can usually be done by finding a rubbery, diffusely enlarged gland, a BMR below 0 per cent, and a normal to high I^{131} uptake. Patients with Hashimoto's disease will have myxedema or will eventually develop it, and the proper treatment is desiccated thyroid. . . . Very little need be said regarding Riedel's type of invasive fibrous thyroiditis, since most physicians will never see a case and, if they do, the proper preoperative diagnosis should be carcinoma.—J. B. Selby, M.D., The Diagnosis and Treatment of Thyroiditis, *The Journal of the Kentucky State Medical Association*, July, 1959.

PROBLEMS IN THE EVOLUTION OF OBSTETRICS

Nicholson J. Eastman, M.D., Baltimore

Obstetrics in the past has been concerned with such questions as the propriety of using anesthesia during labor and the desirability of using sutures to close the uterine wound after cesarean section. Obstetrics in the future will have to face equally fundamental questions. New knowledge is needed in order to solve the problems of premature birth, stillbirth, neonatal death, congenital malformations, and toxemia of pregnancy. Better utilization of existing knowledge is needed also, especially in training the personnel that will be required if adequate, individualized care is to be given to future obstetric patients, in view of the soaring birthrate.

We are commemorating the 100th anniversary of the founding of the Section on Obstetrics and Gynecology of the American Medical Association, which was established in 1859 under the name "Section on Practical Medicine and Obstetrics." Several circumstances serve to make this meeting of our Section a noteworthy occasion. Thus, it is an honor to welcome as our official guest the distinguished president of the Royal College of Obstetricians and Gynecologists.

As we celebrate this centennial, moreover, it may be permissible to note in passing that we are in the best company, for the year 1959 happens to be one *rich in centennials. In the field of English literature,* the year of 1859 saw the publication of Tennyson's "Idylls of the King," of Dickens' "Tale of Two Cities," and of Edward Fitzgerald's translation of "The Rubáiyát of Omar Khayyám." In January of the same year our own Dr. Oliver Wendell Holmes, of puerperal infection fame, began the publication of his "Professor at the Breakfast Table" in the *Atlantic Monthly*. In the sphere of biology, the year of 1859 witnessed the appearance of a volume which has probably had a more profound effect on modern scientific thought than any other single work—Darwin's "Origin of the Species." In an area nearer to our own, Florence Nightingale's "Thoughts on Nursing," published also in 1859, marked the beginning of a new epoch in patient care.

In the fields of literature, biology, and nursing, the year 1859 was an illustrious one. But what, in the same year, was taking place in obstetrics and gynecology? Alas, there was little that was good and much that was bad. Although Semmelweis had demonstrated the cause of puerperal infection 10 years previously, the widespread and vitriolic attacks which were being made on his theory, just 100 years ago, were too much for his sensitive nature and were responsible, as we all know, for his subsequent insanity and death. Likewise, Simpson's introduction of anesthesia into obstetrics had met with denunciation in many quarters, and by 1859 he was spending a goodly part of his time in rebutting the attacks of the many who maintained, on Biblical grounds, that it was sinful so to interfere with natural childbirth, a theme which recalls to mind a certain present-day altercation. Many dedicated physicians of that period, it is true, were devoting their best energies to the improvement of obstetrics; but for the most part, maternity care was in the unclean hands of a vast horde of untrained, ignorant, superstitious, and often alcoholic old women; it was a clandestine and lowly trade rather than a profession.

Early Development of Cesarean Section

To recite the many lifesaving advances which have elevated obstetrics from its low level in 1859 to its present status in 1959 would be to recount a series of events well known to everyone in our specialty, and to review them now would seem unnecessary. But since this is the American Medical Association and since we celebrate today the action taken by certain American worthies in 1859, it would seem appropriate to dwell briefly on the greatest single contribution which has been made by American physicians to obstetrics over the past 100 years. I refer to the well-nigh forgotten role of frontier America in the early development of cesarean section.

Throughout the greater part of the 19th century, cesarean section was the most fatal of surgical procedures. In Great Britain and Ireland, the maternal mortality from the operation had mounted in 1865 to the appalling figure of 85%. In Paris, during the 90 years ending in 1876, not a single successful cesarean section had been performed. The results in Germany, Austria, and Italy were so poor that the newly introduced operation of Porro, which included hysterectomy as well as hysterotomy, was superseding the old and almost universally fatal cesarean section.

From the Department of Obstetrics, the Johns Hopkins University School of Medicine and Hospital.

Chairman's address, read before the Section on Obstetrics and Gynecology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 10, 1959.

The turning point in the development of cesarean section was clear-cut and decisive. It was the appearance in 1882 of a monograph by Max Sänger, then a 28-year-old assistant of Credé in the University Clinic at Leipzig in which the routine employment of uterine sutures was recommended in cesarean section. Prior to Sänger's monograph, uterine sutures in cesarean section had been denounced in Europe as superfluous as well as harmful. In 1770 Andre Levret, the foremost obstetrician of 18th century Paris, had taught that uterine sutures in cesarean section "were not only prejudicial but were absolutely useless because of the prodigious contractions which the uterine muscle undergoes following delivery." Blundell, in his "Principles and Practice of Obstetric Medicine," published in 1840, dismissed the subject with the remark that "sutures to the uterus have not hitherto been in general employ."

Sänger deprecated the growing tendency to abandon the old classic cesarean section in favor of the new Porro procedure, since he believed that careful coaptation of the uterine wound with sutures would obviate all difficulties and permanently establish the superiority of the older operation. But whence came Sänger's idea? Certainly not from his own experience, because his monograph, although reciting *in extenso* the advantages of uterine sutures as he envisaged them, was actually based on only a single successful case in which he had tried them. Nor did it come from his colleagues in the sophisticated centers of Europe, for, as we have seen, sutures were not in favor there. It came, as Sänger very graciously and generously acknowledged, from frontier America, where surgeons working in the outposts of the newly developed Midwest had reported no less than 17 cesarean sections in which uterine sutures had been used. Eight mothers lived and nine died—an incredibly good record for those days. Sänger's monograph includes a table showing the details of these 17 operations. This table was the documentation of his contention and the basis of his monograph. Confirmation of Sänger's convictions in respect to uterine sutures in cesarean section followed quickly. Within a few years suture of the uterus was generally recognized as an indispensable part of cesarean section and the modern operation came into being.

But how did these American surgeons hit upon the idea of using sutures in cesarean section? The first of these operations was performed by a Kentucky surgeon, Frank E. Polin, in December, 1852; he used silver wire sutures, and most of the other 16 sections performed in the Midwest between 1867 and 1880 were done with silver wire sutures. It is significant that in the January preceding Polin's operation, there appeared the celebrated paper of the Alabama surgeon, J. Marion Sims, on the use of silver wire sutures in vesicovaginal fistula and, although Sims did not mention the use of silver wire in cesarean section, it appears that the general idea bore fruit at the hands of these frontier practitioners. By demonstrating the earliest successful type of uterine suture in cesarean section and by furnishing the supporting data for Sänger's monograph, these pioneers made a contribution of immeasurable importance to obstetrics, which we can look back on with pride.

Research Problems of the Future

Having looked back, let us also look forward and ask ourselves, "What are the major problems and challenges which obstetrics in the United States faces in the years to come?" In view of the dramatic reduction in maternal and perinatal mortality which has been achieved during the past few decades, it might seem off-hand that all is well with American obstetrics and that we can now rest on our oars. But all is not well with our obstetrics, and any glib self-satisfaction about its status not only is out of place but can do our specialty irreparable harm. In looking to the future our problems fall quite naturally under two headings: those concerned with the need for new knowledge and those concerned with the best utilization of existing knowledge.

Premature Birth.—In regard to the need for new knowledge, the transcendent problem in obstetrics, not only in the United States but throughout the world, is the cause and prevention of premature birth. More than half of all neonatal deaths are the result of premature birth. One-third of all cases of cerebral palsy are attributable to the same cause. Although some premature births can be explained on the grounds of known factors such as abruptio placentae, placenta previa, multiple pregnancy, and certain maternal complications which demand artificial termination of pregnancy, such as preeclampsia, about 60% of premature births occur without explanation. The importance of these unexplained premature deliveries lies not only in the toll they take in lives of newborn infants and in neuropsychiatric normalcy but in the circumstance that they represent in essence some defect in one of the basic phenomena of reproduction, uterine contractility; there is reason to suspect that this defect in turn stems from some even more basic disorder of the endocrine system. Whatever the cause of premature labor may be, its elucidation and prevention would be the greatest boon that the discipline of obstetrics could confer upon mankind.

Fetal Physiology.—The second most important research problem in obstetrics, as I see it, is fetal physiology and its derangements. This field encompasses, let it be noted, the science of genetics and all that the genes contribute to fetal normalcy or abnormalcy, both physical and mental. It includes also, of course, the many-sided problem of fetal environment—the oxygen supply of the fetus, its nutritional needs, its immunological relationships to the mother, its acid-base balance, its enzyme systems, and many other environmental circumstances essential to fetal well-being. As we all know to our sorrow, any pronounced deviation from the normal in any of these factors may cause stillbirth, neonatal death, and congenital malformations; in sublethal degree it seems probable that they are responsible also for various types of neuropsychiatric disorders. This area is a fairyland for investigation and well worth a lifetime of research to any young man who approaches it with dedicated zeal coupled with working knowledge of a pertinent basic science.

Toxemias of Pregnancy.—As for that age-old enigma of obstetrics, the cause of the toxemias of pregnancy, I would rank it third in importance to the two problems just surveyed. Most maternal deaths from the toxemias today are the result of neglect, either self-neglect by the patient or negligence on the part of the doctor. The majority could be prevented by the timely application of existing knowledge. Preeclampsia per se is not a cause of premature labor but looms large in the over-all picture of prematurity because it often forces the obstetrician's hand to terminate a pregnancy prematurely. I am cognizant of other ways in which the toxemias may prove injurious to both maternal and fetal welfare, but in my opinion the elucidation of the first two problems mentioned would contribute more to human happiness and progress than further knowledge about the toxemias.

Individualized Care of Mothers

The three problems which we have just reviewed represent areas of obstetrics in which new knowledge is urgently needed. Let us turn now to the other phase of our inquiry, namely, how existing knowledge may best be utilized in the United States over the next decade. Here we face a crucial problem. Indeed, on its correct solution we stand or fall. The problem is this: How, with a diminishing personnel and a soaring birth rate, can we hope to give to the mothers of 1970 the meticulous, individualized care which they deserve?

In an article which appeared in the January, 1954, issue of *Children*, published by the Children's Bureau, I set forth this problem in detail with full documentary data, both in respect to the physician shortage which may be anticipated in the 1960's and in regard to the concomitant increase in births. During the intervening five years, the same problem, with new, confirmatory data, has been laid before the American Public Health Association and the American College of Obstetricians and Gynecologists by Dr. John Whitridge Jr. of our clinic. The problem has hence been adequately publicized and is doubtless familiar to you all. Accordingly, a bare statement of the essential facts of the issue will suffice for our present purposes.

The most recent and authoritative estimate of the number of births which will take place in the United States during 1970 is 6 million. This represents a 50% increase in the number of births over those in 1958, and let it be remembered, 1970 is less than 11 years off. Why is a sharp rise in births anticipated? In the mid-40's any overworked obstetrician could have warned his commissioner of public schools to expect a huge increase in first grade pupils around 1952, and exactly this happened. The same obstetrician, on the basis of the soaring birth rates in the 1940's, could have told university authorities to expect an enormous increase in students in the 1960's. On this problem, the Bayne-Jones consultants on medical education and research, in their final report to the Secretary of the Department of Health, Education, and Welfare, as of June, 1958, stated:

> By 1970, the college-age population will be 26 million. This represents nearly a 75 per cent increase above the present level of 15 million, as contrasted with more than a 10 per cent decline (almost 2 million in absolute terms) in this age bracket over the past decade. It should be emphasized that all persons included in this 1970 estimate are now in elementary school.
>
> Drawing from this vastly expanded population base and spurred by strong social and economic incentives, college enrollments will increase steadily and will probably reach 6.4 million by 1970 as contrasted with 3.4 million in 1957. The higher education system of the country clearly faces a decade or more of extreme stress.

Likewise, unless our country is stricken by some major and unprecedented calamity, the marriage bureaus of 1970 will confront a period of extreme stress, because students of college age are rapidly becoming young men and women of marriageable age. More marriages result in more babies. This is the basis for predicting that the volume of maternity work in this country will augment sharply in the 1960's and reach a 50% increase over the present amount by 1970.

Who is going to care for this stupendous number of births? As for medical personnel, all authoritative studies forecast for the 1960's a decrease in the number of physicians in relation to population. On this issue, the Bayne-Jones report makes the following statement:

> A minimum of 14 and as many as 20 new medical schools will have to be built if the existing number of physicians per 100,000 is not to fall. . . . Even if funds in the order of $500 million to $1 billion dollars were made available immediately for construction of new medical schools, it seems certain that the number of physicians per 100,000 population will decline between now and 1970.

This then is the problem—a 50% increase in births between now and 1970 and a diminishing number of physicians in relation to population. In laying this issue before you, it is my main purpose to reiterate its urgency and to implore the several organizations devoted to our specialty to give it serious thought and take appropriate action. Two programs which might conceivably alleviate the shortage of obstetric personnel anticipated for the 1960's are as follows.

Group Practice.—The most practical and realistic way of meeting the problem—one that we know by experience will work—is more group practice. By this is meant the care of obstetric patients by a group of four or five obstetricians who work interchangeably as a unit. For example, on a given day, while obstetricians A and B are seeing antepartum and postpartum patients in the office and handling telephone calls throughout the whole day, obstetrician C is spending a full 24 hours in the delivery suite, managing labors and answering calls throughout the entire night, while obstetrician D is completely off duty for 24 hours. From the viewpoint of a well-ordered life, there would be no night calls whatsoever except for the man on 24-hour duty in the delivery suite; every fourth day each man would be entirely free. From the standpoint of good maternity care, the patients would be assured of the services of a wide awake and alert obstetrician who, when on delivery duty, would be able to give his undivided time to the needs of the parturients. From the viewpoint of the threatened paucity of personnel, four obstetricians in such group practice can handle perhaps eight times the number of cases which any one obstetrician could manage in solo practice. This means a doubling of work output for the group. Finally, there is good reason to believe that programs of this type would make obstetrics a more appealing specialty to our medical graduates.

As we all know, the chief objection to such group practice will come from many patients who insist on care throughout by their favorite obstetrician and by no one else. Although this objection will long be a hindrance to the development of such programs, it may be answered in two ways. 1. Group practice of the type described is not new but has worked successfully and to the complete satisfaction of patients in many localities. 2. Little by little, expectant mothers must be led to understand that any competent obstetrician who is wide awake and alert is a safer and more trustworthy man than the best obstetrican in the world who is harassed by overwork and groggy from lack of sleep.

Obstetric Assistants.—The work output of a group of obstetricians could be increased in both quantity and quality if they could have the round-the-clock assistance of a few graduate nurses who have received special training in the conduct of normal pregnancy, labor, and the puerperium. By training is meant not less than eight months' full-time clinical tutelage under the supervision, control, and accreditation of obstetricians. The best appellation for such auxiliary personnel would be "obstetric assistants." With proper training such nurses would be competent to perform, if need be, the following services: in antepartum care—history taking, blood pressure determinations, venipunctures, abdominal palpation, fetal heart observations, and attention to the more common complaints such as nausea, heartburn, constipation, and excessive weight gain; in labor—in addition to the procedures just mentioned, they would be available to carry out rectal examinations, emotional support of the parturient, and, if need be, nearly the entire conduct of labor except actual delivery. This would be undertaken only in an emergency, but they should be trained for this eventuality. If, at any time, the slightest abnormality developed, the obstetrician would be notified immediately. It must be emphasized that these obstetric assistants would at all times serve under the direct supervision and control of obstetricians, and always in hospitals or in doctors' offices.

The term "nurse midwife" is often applied to this type of personnel, which I have designated, by preference, as "obstetric assistants." Most nursing groups and organizations devoted to the development of these obstetric assistants much prefer the term "nurse midwife." Moreover, many nurses so trained choose to serve in underdeveloped countries and can be accredited by such international bodies as the World Health Organization only as "nurse midwives." For these two reasons this appellation is gaining currency despite the stigma which the word "midwife" carries in the United States. But, by whatever name they may be called, my own experience with these nurses indicates beyond question that they have much to contribute to maternity care in the United States and that, when the need exists, they can do a great deal to relieve overworked obstetricians of routine burdens.

But, as indicated, it is my purpose to pose this question of paucity of obstetric personnel in the 1960's rather than to answer it. It is an urgent problem, because personnel cannot be developed overnight. In addition, the need for more maternity beds requires investigation, because already, in most hospitals, the stay of maternity patients has been reduced to a shameful and irreducible minimum. If steps are not taken to meet these two problems, the problem of obstetric personnel and the problem of hospital facilities over the next decade, and if the mothers of 1970, just 11 years hence, are neglected because of inadequate personnel and shortage of maternity beds, their neglect tomorrow will be the direct result of our apathy and indecision today.

MANAGEMENT OF URETERAL INJURIES

William J. Staubitz, M.D., Imre V. Magoss, M.D., Melbourne H. Lent, M.D., Eugene M. Sigman, M.D.
and
Oscar J. Oberkircher, M.D., Buffalo

Ureteral injuries occurring in 22 patients during surgical and irradiation therapy of abdominal cancer were studied, with the intention of improving the management of this operative hazard. The most frequent type of damage was physical trauma from accidents of surgical technique: puncture, crushing, or ligation of the ureter. Fibrosis, secondary to radiation of tumors close to the ureters, occurred in three patients. A majority of the injuries were diagnosed and repaired at the time they occurred; this is the best plan of management. When an injury was not noticed, the signs and symptoms usually observed in the immediate postoperative period were pain, fever, azotemia, anuria, and urine draining from an abnormal site. A blood-free operative field and careful surgical dissection will keep accidents at a minimum, but if one does happen the surgeon must be prepared to repair the ureter, with varied techniques, depending on the site, type, and extent of the injury. Preoperatively an outline of the urinary tract should be obtained (by roentgenography) and indwelling ureteral catheters inserted if possible.

Injury to one or both ureters has been a hazard in surgery of the pelvic organs since surgeons first began operating in this area. These injuries have become more prevalent during the last few decades, since surgeons have adopted a more radical approach to therapy of malignant disease involving the pelvic organs and colon. This paper reports a study of the management of ureteral injuries occurring in an institution in which advanced malignant lesions are treated by both extensive surgery and irradiation.

The incidence of ureteral injuries as reported by different authors varies between 0.5 and 10%.[1] The exact incidence has never been established, because many of these surgical accidents may not be reported and also because unilateral injuries may remain asymptomatic and, consequently, may not be recognized.

We shall not attempt to establish a rate of ureteral injury in this study because, while complete pretherapy and post-therapy urologic evaluations are done routinely on all gynecologic patients, they are done only when requested on patients of other services. Therefore, it is possible that certain patients undergoing rectocolonic surgery may have suffered unilateral injuries which have not manifested themselves clinically.

Causes and Types of Injury

Abdominal and pelvic surgical procedures are regarded as the most frequent cause of ureteral injury. Anatomically, the ureters are well protected from external trauma; however, their proximity to the large intestine and pelvic viscera makes them vulnerable to surgical and radiologic trauma.

In the pathogenesis of these surgical accidents five factors appear significant: (1) control of hemorrhage after a slipped or broken ligature, with hasty attempts to reclamp the usually retracted bleeding vessel without direct vision; (2) removal of large tumors, when the size of the lesion itself or the operative manipulation may alter the normal anatomic landmarks; (3) interference with the blood supply, without direct injury to the ureter; (4) closure of the posterior peritoneum, with kinking or displacement of the ureters (subsequent healing and scarring may result in further obstruction, necrosis, and/or fistulas); and (5) needle punctures, necrosis from clamps, and the indiscriminate use of transfixion sutures without the benefit of direct vision.

Our series of 23 ureteral injuries occurred in 22 patients. The highest incidence of injury followed the Wertheim radical hysterectomy for carcinoma of the cervix. Among eight patients with nine ureteral injuries one patient suffered a bilateral injury and seven patients had unilateral involvement. The right ureter was injured in three instances and the left in six. Five injuries resulted from necrosis, the exact cause of which was never determined but was thought to be interference with the blood supply; three injuries were caused by transection and one by ligation of the ureter.

Surgery of rectocolonic lesions, both malignant and benign, accounted for five accidents to the ureter. Three injuries occurred during a Miles' abdominoperineal resection for tumor of the recto-

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From Roswell Park Memorial Institute, and the Department of Urology, University of Buffalo School of Medicine.

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sigmoid: two ureters were transected and one developed necrosis because of angulation. The fourth injury occurred when a ureter was transected during an anterior resection for carcinoma of the sigmoid colon and the fifth when a ureter was transected during surgery for diverticulitis of the descending colon.

Four injuries were caused by radiation therapy, both external and interstitial, for malignancy of the cervix and vagina. Specimens obtained from the sites of obstruction in these cases indicated fibrosis only.

The five remaining accidents occurred during pelvic surgery for lesions of the female genital tract. In one case a left ureter was ligated during removal of a large granulosa cell tumor of the ovary. Four injuries occurred during hysterectomy for benign lesions: the right ureter was ligated in three cases and suffered a crushing injury in one.

Symptoms and Diagnosis

The most common symptom of ureteral injury, not recognized at the time of surgery, is abnormal urinary leakage. Of 16 cases in which it was present there were 11 ureterovaginal fistulas, 3 ureteroperineal fistulas, and 2 ureterocutaneous fistulas (draining through the abdominal wound). Other symptoms noted in these unrecognized cases were pain in five cases, fever in three, and azotemia in one. Anuria is the predominant symptom if both ureters have been ligated. This situation, however, was not present in any of the cases being reported.

TABLE 1.—*Management and Results of Ureteral Injuries Recognized at Time of Surgery*

	Injury			
Primary Disease and Operation	Side and Site	Type	Corrective Operation	Result
Carcinoma of cervix; Wertheim's	Left lower ⅓	Cut	End-to-	Good
Diverticulitis of sigmoid; abdominoperineal resection	Left lower ⅓	Cut	End-to-	Good
Carcinoma of sigmoid; anterior resection	Left middle ⅓	Cut	End-to-	Good
Fibroid uterus; hysterectomy	Right lower ⅓	Ligation and crushing	End-to-	Good
Carcinoma of rectum; abdominoperineal resection	Left lower ⅓	Cut	End-to-end anastomosis with intubation (silk)	Poor
Carcinoma of cervix; Wertheim's	Right lower ⅓	Cut	End-to-end anastomosis with intubation, with T tube	Poor
Carcinoma of cervix; Wertheim's	Right lower ⅓	Cut	End-to-end anastomosis with intubation, with T tube	Poor

Injury to a ureter at the time of surgery is often diagnosed by direct observation; otherwise, diagnosis must await the onset of symptoms. When there is no urinary output after pelvic surgery, bilateral ureteral ligation should be suspected. This condition must be differentiated from acute renal shutdown due to shock, hemorrhage, or transfusion reaction. When bilateral obstruction is suspected cystoscopy, with passage of ureteral catheters, should be done immediately. If the catheters in the ureters meet obstruction on both sides, a diagnosis of bilateral ureteral injury must be made. If there is no ureteral obstruction, acute renal shutdown is the more likely diagnosis.

Postoperative symptoms of abnormal vaginal, perineal, or abdominal wall leakage, as well as flank pain, fever, or increasing azotemia, indicate possible ureteral injury, and more detailed diagnostic studies should be made. Intravenous pyelography will show whether the kidneys are functioning and whether ureteral and pelvic dilatation is present on one or both sides. It may even demonstrate an abnormal course of one of the ureters. Any abnormal pyelographic finding suggests ureteral injury on the side of the abnormality.

Instillation of indigo carmine into the bladder will demonstrate whether a vesicovaginal or vesicoperineal fistula is present. In either case, the dye is seen coming through the abnormal tract. If there is urinary drainage from the vagina or perineum, but none of the instilled dye comes through, a ureteral fistula may be tentatively diagnosed.

Cytoscopy in the case of a vesical fistula will demonstrate an actual opening in the bladder or may demonstrate necrosis or marked edema in the suspected site. When a ureteral injury or fistula is present, the bladder may appear normal or show only the usual postoperative edema of a mild degree. In the case of a ureteral fistula due to transection or necrosis the ureteral catheter usually meets obstruction at the point of injury. Occasionally, the catheter finds its way into the fistulous tract and presents itself through the abnormal opening in the vagina, perineum, or abdominal wall. Radiopaque medium injected through the catheter in the obstructed ureter may find its way into the fistulous tract to be demonstrated roentgenographically.

An incomplete injury or loose ligation of the ureter may allow the catheter to go through the obstructed ureter to the kidney pelvis. Retrograde pyeloureterograms may then demonstrate the point of partial obstruction. If at all possible, retrograde studies of both kidneys should be done to rule out the presence of bilateral injury. Diagnosis of ureteral injury and its exact location thus requires the use of the entire urologic and radiologic armamentarium.

Management

The ureteral injuries in this series can be placed into two categories: those recognized at the time of surgery and repaired immediately (shown in table 1) and those unrecognized and repaired from two weeks to two years later (shown in table 2). Management of most of these accidents was supervised by the urologic service. However, a few cases recognized at the time of surgery were managed without urologic consultation.

Seven injuries were recognized and treated immediately. Five were managed by end-to-end anastomosis and intubation, with use of a no. 6 ureteral catheter. The technique used in four cases was as follows: The cut ends of the ureter were trimmed obliquely to prevent a circular constricting scar and then approximated without tension at the anastomosis. With interrupted 0000 chromic catgut on an atraumatic needle, the sutures were limited to the adventitial and muscle layers, an effort being made to avoid the epithelium. In all four cases the site of anastomosis was drained, and the splinting catheter was removed on the seventh postoperative day. All four patients had a successful outcome. Figure 1 illustrates the results in one of these cases. The fifth patient was treated with a similar technique, except that silk instead of chromic catgut was used and the site of anastomosis was not drained. Postoperatively this patient developed a persistent ureteroperineal fistula from the site of anastomosis and ultimately required nephrectomy.

The remaining two patients whose cases were recognized and treated immediately were managed by an end-to-end anastomosis over a T tube, with the long arm brought through the anastomosis and the abdominal wall. Both patients developed persistent ureterocutaneous fistulas and later required nephrectomy.

Sixteen ureteral accidents were not immediately recognized. Of these 12 were surgical accidents and 4 developed after radiation. These cases were managed by different techniques determined by the type, site, and extent of the injury and the status of kidney function. In each case, at the time of exploration and ureteral repair, a biopsy specimen was taken from the site of injury to determine the presence or absence of malignancy.

TABLE 2.—*Management and Results of Ureteral Injuries Unrecognized at Time of Surgery*

	Injury				
Primary Disease and Therapeutic Procedure	Side and Site	Type	Interval Before Operation	Corrective Operation	Result
Carcinoma of cervix; radiation and Wertheim's...	Left lower ⅓	Not known	10 wk.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's.................	Left lower ⅓	Not known	3 mo.	Ureteroneocystostomy	Good
Carcinoma of rectum; abdominoperineal resection	Right lower ⅓	Not known	3 mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; radiation..................	Left lower ⅓	Fibrosis	3 mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's.................	Left lower ⅓	Not known	2½ mo.	Ureteroneocystostomy	Good
Carcinoma of cervix; Wertheim's.................	Left lower ⅓	Not known	1 yr.	Ureteroneocystostomy	Good
Carcinoma of rectum; abdominoperineal resection	Right lower ⅓	Cut	2½ wk.	Ureteroneocystostomy	Good
Carcinoma of cervix; radium therapy.............	Right lower ⅓	Fibrosis	2 wk.	Nephrostomy followed by ureteroneocystostomy	Good
Fibroid uterus; hysterectomy....................	Left lower ⅓	Crushing	2 mo.	1. Ureteroneocystostomy 2. Ileal substitute for lower ⅔ of ureter	Poor Good
Fibroid uterus; hysterectomy....................	Right lower ⅓	Not known	4½ mo.	Ureteroneocystostomy and nephrectomy	Poor
Ovarian granulosa cell tumor; right oophorectomy and excision of cervix..........................	Left lower ⅓	Ligation	15 days	Deligation, end-to-end anastomosis, and intubation	Good
Carcinoma of cervix; radiation therapy..........	Right lower ⅓	Fibrosis	2 yr.	Ureterolysis	Good
Cervicitis and ovarian cyst; removal of cervical stump and salpingo-oophorectomy..............	Right middle ⅓	Ligation	3½ wk.	Deligation and ureterotomy with T tube	Good
Carcinoma of cervix; Wertheim's.................	Right, site not known	Not known	6 mo.	Nephrectomy	Poor
Epidermoid carcinoma of vagina; radiation therapy and vaginectomy.......................	Left middle ⅓	Not known	7 mo.	Nephrostomy followed by ureterolysis and intubation	Poor
Carcinoma of cervix; Wertheim's.................	Left lower ⅓	Not known	8 wk.	Cutaneous ureterostomy followed by nephrectomy	Poor

Ureteroneocystostomy was used as the only reparative treatment in nine cases. This was possible because the injuries were low in the ureter and close to the bladder. Preliminary nephrostomy was done in one of these patients to help control severe infection and to improve kidney function prior to ureteral repair.

Ureteroneocystostomy was done by simply freeing the affected ureter from the surrounding tissues for several centimeters above the site of injury (fig. 2). The ureter was then divided just above the injury (fig. 2*A*). The cut end of the ureter was trimmed, split, and brought through a stab wound (fig. 2*B*) in the bladder wall as close as possible to the trigone (fig. 2*C*). The split edges of ureter were fixed to the bladder wall by fine chromic catgut mattress sutures (fig. 2*D*). The ureter was also fixed to the outer bladder wall with several anchoring sutures through the adventitial and muscle layers (fig. 2*E*). A no. 6 or no. 7 catheter was then passed up the ureter to the kidney pelvis, brought through a midline stab wound, and anchored to a suprapubic drainage tube (fig. 2*F*). This splinting catheter was removed 7 to 10 days later. Of these nine cases results were good in eight and one was a failure, requiring later nephrectomy. The remaining seven patients with unrecognized cases were managed by seven different techniques, as listed in table 2.

Results

The results obtained in this series of 22 patients with 23 ureteral injuries are summarized in tables 1 and 2. There were 15 good and 8 poor results. No operative mortality was associated with the ureteral repairs. Whenever a case ended in a nonfunctioning kidney or nephrectomy, the result was classified as poor. The results were considered good only if, after a sufficient follow-up period, the renal function of the involved side was preserved and the patient remained asymptomatic.

Seven ureteral injuries were recognized and treated immediately. Results were good in four cases. Unsatisfactory results occurred in three cases in which some of the basic principles of urologic surgery were not observed; these errors included the use of nonabsorbable suture material, T-tube drainage through the anastomosis, and failure to drain the site of repair.

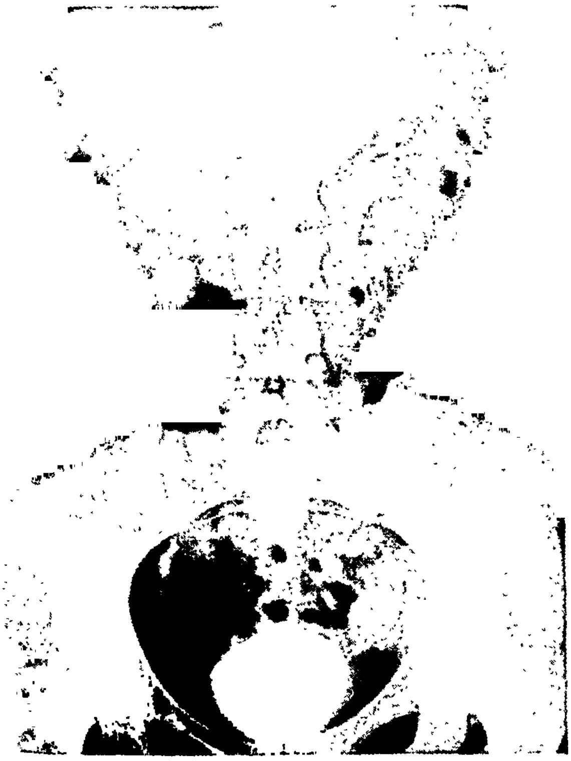

Fig. 1—Postoperative excretory pyelogram of patient after repair of left ureteral injury by end-to-end anastomosis and intubation. Note normal appearance of left collecting system and ureter.

The unrecognized cases in this series were repaired after intervals of two weeks to two years, the average interval being six months. Results were good in 12 cases and unsatisfactory, resulting in a nonfunctioning kidney or necessitating a nephrectomy, in 4. With one exception, the good results were obtained in cases repaired after an average interval of three months and the bad results after an average interval of five months. The exception occurred in a patient with radiation damage, with vaginal urinary leakage for two years. A satisfactory repair was obtained.

Among the 16 unrecognized cases the lower third of the ureter was involved in 13 cases, the middle third in 2, and in one case the site was unknown. Ureteroneocystostomy was carried out in 10 of these patients and good results were obtained in 8. Of the two failures the kidney of one patient was saved by an ileal loop substitute of approximately two-thirds of the ureter during a second reparative operation, and a good result was obtained. The other ureteroneocystostomy which failed, so that the patient ultimately required nephrectomy to stop the urinary leakage, was classified as a failure. The three remaining good results occurred in injuries of the middle part of the ureter in one case and the lower part in two cases. Deligation and an end-to-end anastomosis with intubation was successful in one case. Ureterolysis without intubation was successful in another. The third case was managed by deligation and intubation with a T tube. The long arm of the T tube was brought out through a ureterostomy above the site of injury, and a good result was obtained.

Results were poor in four cases. One involved a ureteroneocystostomy and has been discussed above. A second patient was seen six months after surgery, when urologic study revealed a nonfunctioning, infected, hydronephrotic kidney. No attempt was made to repair the injury and nephrectomy was performed to stop the urinary leakage. In a third patient an emergency nephrostomy was required to combat infection; later, ureterolysis and intubation failed to stop the leakage and a nephrectomy was required. The fourth patient had a cutaneous ureterostomy after exploration revealed a damaged segment of ureter approximately 6 cm. from the bladder and too short for end-to-end anastomosis. The surgeon chose cutaneous ureterostomy and later nephrectomy rather than use of an ileal loop or bladder flap to bridge the defect.

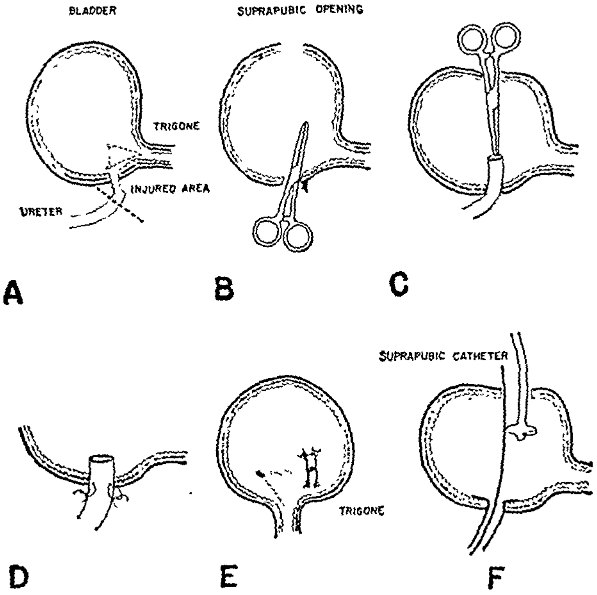

Fig. 2—Technique for ureteroneocystostomy: *A*, ureter is severed proximally to injured area; *B*, with blunt instrument, stab wound is made through bladder wall as close to ureteral orifice as possible; *C*, ureter is pulled into bladder through stab wound; *D*, fine chromic catgut sutures anchor adventitia of ureter to serosa of bladder; *E*, "fish-mouthed" ureter is anchored to bladder epithelium with fine chromic catgut sutures; *F*, ureteral catheter splinted.

Comment

Although ureteral injuries will continue to occur, even with the most experienced surgeons, prophylactic measures can appreciably decrease their incidence.

Preoperative Phase.—Preoperative evaluation of the genitourinary tract by means of excretory and/or retrograde pyelography will reveal such aberrations as congenital anomalies, ureters deviated from their normal course by large tumors or inflammatory masses, and primary incidental urologic diseases. Any one of these factors will render the ureter more susceptible to surgical trauma.

In this institute, indwelling ureteral catheters have been inserted preoperatively only at the request of the various surgical services. Whenever this preoperative measure was employed, no ureteral injury occurred. We believe that the preoperative insertion of indwelling catheters is advisable in all pelvic surgical procedures.

Operative Phase.—The failure to recognize a ureteral injury during surgery eliminates the most favorable time for repair. The longer the time interval between obstruction and repair the less chance the kidney has for recovery.

The technique of repair depends on the site, type, and extent of the injury. End-to-end anastomosis with intubation and ureteroneocystostomy has given us our best results. Use of the T tube as a splinting and drainage catheter after ureteral repair is not recommended and should be avoided; however, if one insists on its use, the long arm should be brought out through a separate ureterostomy proximal to the anastomosis and not through the suture line.

Nonabsorbable suture material should never be used in urologic surgery where it may be in direct contact with urine flow. The site of anastomosis should be adequately drained. Anastomosis should never be attempted with the ureters under tension.

During the dissection and isolation of the ureters care must be exercised to leave the ureteral adventitia intact, since it has an extremely rich collateral blood supply.

Postoperative Phase.—With a preoperative base line of the genitourinary tract available, the postoperative evaluation of these patients enables us to recognize asymptomatic ureteral injuries. Many authors agree that entablishing adequate drainage within two weeks may result in recovery of the completely obstructed kidney. However, when a urinary fistula occurs, some form of drainage is established which maintains partial renal function and provides more time for repair. Nevertheless, the physician may be lulled into a false sense of security when the fistula spontaneously ceases to drain, for in many such instances this represents the end-result of a ureteral injury, namely, a nonfunctioning kidney.

Conclusions

Because of the anatomic arrangement of the lower part of the ureter there is always danger of injury to it in extensive surgery or irradiation of the pelvis. Preoperative intravenous pyelograms and preoperative insertion of ureteral catheters are the most useful aids in preventing ureteral injuries. The use of these procedures indicates that the operator is alerted to possible ureteral injuries. Early recognition and early repair give the best result.

In the immediately recognized ureteral injuries end-to-end anastomosis with intubation is the preferred treatment. Ureteroneocystostomy gives the best results in the delayed repair of fistulas involving the lower part of the ureter. Adequate drainage and control of infection are essential. Postoperative observation is necessary, since ureteral stricture or loss of kidney function may develop.

40 W. North St. (2) (Dr. Staubitz).

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ACCIDENT PREVENTION IN CHILDHOOD.—Fatal accidents now take a toll each year of about 4,700 children past their infancy but not yet of school age. These deaths account for more than one fourth of the total at ages 1-4. At this early stage of life, accidents cause about twice as many deaths as pneumonia and nearly 3 times the number from cancer in all its forms. This is far from a satisfactory situation even though it represents a substantial improvement over that of only a few years earlier. . . . The primary responsibility for the control of mishaps among pre-school children rests upon their parents. They must provide good supervision, remove hazards, teach simple safety measures, and set good examples at all times. However, physicians, especially pediatricians, are making major contributions in advising parents on the principles of accident prevention and by promoting community programs for child safety.—The Peak in Family Responsibilities, *Statistical Bulletin*, Metropolitan Life Insurance Company. August, 1959.

ACUTE LARYNGEAL OBSTRUCTION IN CHILDREN

Francis W. Davison, M.D., Danville, Pa.

When children develop acute laryngeal obstruction it is important to know promptly whether bronchoscopy and tracheotomy are called for. During a 14-year period 140 cases of acute laryngotracheobronchitis have been treated. Tracheotomy was found necessary in 28 cases. During 1958 steroid therapy was used in 13 cases of acute subglottic laryngitis and, in every case this obviated the need for tracheotomy. A case history illustrates the rapid improvement induced by hydrocortisone given by intravenous drip in infectious subglottic laryngitis in an atopic child. The history of a second case of subglottic laryngitis illustrates the extreme degree of crusting that can occur and the promptness of relief when crusts are removed by bronchoscopy and respiration is eased by tracheotomy. In the experience of the author prompt differential diagnosis, followed by modern methods of treatment, has been lifesaving in nearly every case of acute laryngeal obstruction in children.

Croup is the diagnosis most frequently made when a physician sees a child with acute laryngeal obstruction. This diagnosis is inadequate because there are at least six different causes of acute obstruction. Fatalities can be prevented if the correct diagnosis is made early and if proper therapy for the cause of the obstruction is promptly initiated. Terminology is important. I prefer a classification which indicates the anatomic site of the obstruction as well as the cause of the obstruction, because it fixes attention on the factors that must be promptly corrected if unnecessary tragic fatalities are to be prevented.

Some years ago I advocated [1] the following classification of acute laryngeal obstruction in children: (1) acute obstructive supraglottic laryngitis (acute epiglottitis, edematous septic laryngitis, influenzal laryngitis, and edema of the glottis); (2) supraglottic allergic edema (angioneurotic edema); (3) laryngeal diphtheria (membranous croup, true croup, and diphtheritic croup); (4) subglottic allergic edema (spasmodic croup, spasmodic laryngitis, false croup, catarrhal spasm of the larynx, and laryngismus stridulus); (5) acute laryngotracheobronchitis (subglottic laryngitis, and nondiphtheritic croup) and virus croup [2]; and (6) foreign body in the larynx or upper trachea.

I was glad to see this classification copied in one of the pediatric textbooks,[3] because pediatricians, who often see these children first, must recognize the different types of obstruction and must know promptly when to call an otolaryngologist who has the ability to introduce a bronchoscope and perform a tracheotomy.

Each of these forms of acute laryngeal obstruction causes the classic symptoms of stridor, retraction of the soft tissues above the clavicles and in the epigastrium during inspiration, and elevated pulse and respiratory rates, but the urgency of treatment and type of treatment depend on the type of disease present.

Acute Obstructive Supraglottic Laryngitis

Acute obstructive supraglottic laryngitis (acute epiglottitis) [4] is a term applied to inflammation involving chiefly the epiglottis and aryepiglottic folds. It is a clinical entity and should be distinguished from all other types of acute laryngeal obstruction because it develops with great rapidity. Only four or six hours may elapse from the first symptom until the time tracheotomy is urgently needed. Failure to recognize this fact may lead to a fatality, as is evidenced by the following case report.

Case 1.—This child, a male, aged 2½ years, was in good health until eight hours before admission, when he had an emesis and was noted to have a temperature of 103 F (39.4 C). Two and one-half hours prior to his admission on the pediatric service, his respirations became noisy and rapid. The pulse rate on admission was 140 and the respiratory rate 56 per minute. While a lumbar puncture was being attempted, the child ceased breathing. An emergency tracheotomy was performed, but respirations were not reestablished. One hour had elapsed from the time of admission until the time of death. Much work had been done, as evidenced by the large number of laboratory reports in the chart, but the child died because the attending physician did not know that a child with epiglottitis can breathe reasonably well sitting up and yet breathing can become totally obstructed by the swollen supraglottic structures when the child is placed in the horizontal position, which was used to permit performance of the lumbar puncture. For those who place great faith in the importance and veracity of cultures, I cite the following facts. This

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From the Department of Otolaryngology and Broncho-Esophagology, the George F. Geisinger Memorial Hospital and Foss Clinic.

Read before the Section on Laryngology, Otology, and Rhinology at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 9, 1959.

child's nose culture showed Diplococcus pneumoniae, the throat culture showed a beta hemolytic streptococcus, and the blood culture showed Hemophilus influenzae.

Comment.—The clinical picture is usually recognizable without direct laryngoscopy, and direct laryngoscopy should be done only by someone who has at hand a 3.5-mm. or 4-mm. bronchoscope and knows how to introduce it rapidly and safely. The fiery red, tremendously swollen epiglottis can be seen if the child is examined while being supported and restrained in the sitting position if the examiner uses a headlight and a small, child-size metal tongue blade. If it is done skillfully and quickly there will be only momentary increase in dyspnea. These children should not be restrained in the supine position.

With this type of obstruction there is stridor on inspiration and a coarse, fluttering sound during expiration, due to vibration of the swollen aryepiglottic folds. A croupy cough is never present because a croupy cough is due only to subglottic swelling. I have never seen epiglottitis and subglottic edema in the same patient. Respirations are apt to be relatively slow in proportion to the pulse rate, because the patient has learned that rapid or forceful inspiration sucks the edematous aryepiglottic folds into the larynx and thus increases the obstruction. Pale cyanosis is often present. The shock-like picture described by some authors is, in my opinion, due to hypoxia. I say this because it clears up immediately after introduction of a bronchoscope and performance of tracheotomy. The technique of tracheotomy is well described by Galloway.[5] Oxygen is no substitute for tracheotomy but may be used as a temporary measure. These children have inspiratory stridor as well as the coarse fluttering sound during expiration, but there is seldom true hoarseness. As Miller[4] says, these children insist on sitting up and extend the head forward in order to increase the greatly narrowed supraglottic airway. Older children will complain of pain in the throat. Swallowing is very difficult, so saliva drools from the mouth. Use of a humidified tent is not necessary for patients having supraglottic laryngitis, unless a tracheotomy has been done.

This type of infection is usually, but not always, due to H. influenzae, type B. Therefore, after tracheotomy, the most important part of the treatment is use of streptomycin given intramuscularly, 20 mg. per pound of body weight per day in divided doses every six hours, and penicillin given intramuscularly. I prefer fortified procaine penicillin G, 1 million units given intramuscularly every six hours. The antibiotics selected should be given by injection to insure prompt absorption. There was only one death in my series of 20 cases of epiglottitis, and that was due to delayed tracheotomy. Ten patients required tracheotomy.

Supraglottic Allergic Edema

Allergic edema involving the supraglottic structures (angioneurotic edema) can develop with great rapidity and present exactly the same clinical picture as that caused by acute supraglottic laryngitis, but direct laryngoscopy shows a pale watery edema of the epiglottis and the aryepiglottic folds in contrast to the fiery red edema seen when the obstruction is due to acute supraglottic laryngitis. Allergic edema will usually respond quickly to parenteral administration of epinephrine, but in one case it was necessary to insert a bronchoscope and leave it in position for a period of 15 minutes until the edema had subsided sufficiently to permit unembarrassed respiration.

In one case the acute supraglottic allergic edema in a 6-year-old boy was the result of antitetanic serum given 10 days previously. The edema subsided quickly in response to 0.2 cc. of 1:1,000 aqueous solution of epinephrine given subcutaneously.

Laryngeal Diphtheria

Laryngeal diphtheria sometimes occurs when there is no membrane visible on the pharynx or tonsils so that accurate diagnosis must depend on direct laryngoscopy confirmed by smears and cultures. However, certain points in the history and physical examination should lead the examiner to suspect its presence. Usually diphtheritic laryngitis is slow in development, with a lapse of two or three days from the onset of hoarseness until dyspnea is sufficiently marked to require tracheotomy. Usually the temperature is not high and may be no more than 100 or 101 F (37.8 or 38.3 C). The cry is hoarse because normal vibration of the cords is hampered by the presence of membrane.

A specimen for smears and cultures can be most conveniently obtained by using an aspirating collector through a direct laryngoscope. If there is a membranous type of exudate or if direct smears show positive results for the presence of diphtheria organisms, it is advisable to give antitoxin without waiting for the culture report. Further details of the management of diphtheritic cases may be found in any of the standard pediatric textbooks.

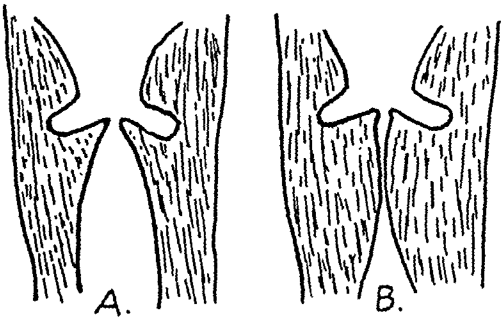
Subglottic Allergic Edema

Characteristically, children with subglottic allergic edema (spasmodic croup, laryngeal stridor, spasmodic laryngitis, or false croup) awaken at night with dyspnea, croupy cough, and inspiratory stridor. They usually have been quite well the preceding day or may possibly have had a little rhinitis but no fever. By morning the symptoms have cleared up, only to recur the next night and possibly for several succeeding nights. For generations this clinical picture has been referred to as spasmodic croup, the inference being that the obstruction is due to adductor spasm of the vocal cords. This concept is erroneous for the following reason.

The sound of the croupy cough is identical with that produced by the subglottic swelling seen by direct laryngoscopy in cases of acute laryngotracheitis.

The diagrams in the figure show coronal sections of a normal larynx and the location of the subglottic swelling which produces a croupy cough. This swelling may be due to a transient allergic edema or to the indurated submucosal inflammation present in cases of infectious subglottic laryngitis.

In a few cases of so-called spasmodic croup that I have observed in hospital practice, direct laryngoscopy showed pale watery edema of the subglottic tissues, and the obstructive symptoms cleared up within 15 minutes after subcutaneous administration of 0.2 cc. of aqueous solution of epinephrine. The rapid onset and later improvement in one to four hours in these patients having subglottic allergic edema is quite comparable to the transitory nature of hives in the skin. Croup has been referred to as a manifestation of allergy by Vaughan,[6] Rowe,[7] Cohen,[8] Spain,[9] Urbach,[10] and other physicians who are experienced in dealing with allergic persons.



A, coronal section of a normal larynx. *B*, coronal section showing subglottic swelling, which is only cause of croupy cough; it may be due to allergic edema or to indurated submucosal swelling of acute laryngotracheitis.

I have suggested the term subglottic allergic edema for this malady because it is descriptive of both the anatomic location and the etiology. It is distinguished from other forms of obstructive laryngitis by its sudden onset and by the complete or almost complete remission of symptoms during the daytime.

All physicians to whom I have suggested the use of epinephrine for treatment of nocturnal spasmodic croup have reported that it was effective and have said in addition that use of diphenhydramine (Benadryl) hydrochloride saved them many night calls for children who were subject to croup.

Acute Laryngotracheobronchitis

Acute laryngotracheobronchitis (subglottic laryngitis) most often begins as primary subglottic laryngitis. The children have a dry, croupy cough and inspiratory stridor produced by subglottic swelling. In almost all cases the sound of the cry is clear, indicating that the edges of the vocal cords are normal and free from membrane. The temperature varies from 100 to 105 F (37.8 to 40.5 C). The dyspnea becomes progressively worse over a period of one to seven days before it is severe enough to require admission of the child to a hospital.

Many of the patients have had previous head colds. Head colds cause nasal obstruction and mouth breathing so that the extremely dry indoor air in winter impinges directly on the larynx without having previously been moistened by passage through the nose.

The pathological changes observed by means of direct laryngoscopy and bronchoscopy are redness and swelling of the lateral walls of the trachea just below the vocal cords so that the subglottic space is reduced to an anteroposterior slit 1 to 2 mm. wide. Often the subglottic tissues are coated with a layer of dry, rough, gray adherent exudate which extends downward 0.5 in. below the level of the cords and increases the obstruction. Usually this exudate does not have the appearance of diphtheritic membrane. The swelling of the subglottic tissues is firm and indurated as is demonstrated by the fact that it requires considerable pressure to introduce even a 3.5-mm. bronchoscope. This subglottic swelling is not due to simple watery edema but to infiltration of the submucous tissues of the conus elasticus with inflammatory cells, as postmortem examinations have shown. Holinger[11] has called our attention to the fact that the subglottic tissues are surrounded by a firm cartilaginous ring, so that inflammatory swelling can take place only at the expense of the airway.

Our cultures and those of many other observers[12] indicate that any of the pathogenic gram-positive cocci can be the bacterial agent responsible for this disease. Moreover, smears made from the intratracheal exudate aspirated through the bronchoscope introduced just prior to tracheotomy showed gram-positive cocci mixed with neutrophils, so it seems unnecessary to postulate a virus infection as the cause of the disease. In addition, most patients have shown such prompt response to treatment with penicillin that it seems evident that the infection is due to penicillin-sensitive organisms. The viral origin of acute subglottic laryngitis has been stressed by Rabe.[2] It is, of course, possible that a virus initiates the infection. This is an academic concept of no practical importance because it does nothing to help us prevent or cure the infection.

Treatment

The most urgent part of treatment is relief of airway obstruction. The patients are placed immediately in a humidified oxygen tent. The relative humidity should be at least 90%, with the temperature maintained between 70 and 75 F.[13] The high humidity helps to maintain the fluidity of the tracheobronchial secretion and tends to soften the crusts adherent to the subglottic mucosa so that they can be coughed out. We frequently see rapid improvement in the airway within two hours after a child has been placed in a humidified tent.[14] The nurse is instructed to count and record the pulse and respiratory rates every 15 minutes. I regard a pulse rate of over 140 or a respiratory rate of over 40 per minute as a danger sign. If the pulse and respiratory rates continue to increase or do not decrease during the first three hours after the child is placed in the humidified tent, it is probable that tracheotomy will be required. If there is obvious urgent dyspnea accompanied by the pale gray type of cyanosis at the time of admission, a small bronchoscope is introduced and tracheotomy performed immediately before the child is placed in the tent.

The following case report illustrates the extreme degree of crusting that can occur and shows why introduction of a flexible endotracheal tube is not as satisfactory as introduction of a bronchoscope just prior to tracheotomy.

Case 2.—An 8-year-old boy was admitted in an almost moribund state. He was pale and irrational and had rapid shallow noisy respiration. There was marked indrawing of the soft tissues in the suprasternal notch and in the epigastrium with each inspiratory effort. Immediate direct laryngoscopy showed marked redness and swelling of the lateral walls just below the vocal cords. Hard, dry adherent crusts almost filled the remaining airway. A 5-mm. bronchoscope was introduced, and the crusts were removed with aspirator and forceps. An orderly tracheotomy was then performed. After five minutes, the boy sat up and drank a cup of water. Cultures from the endotracheal exudate showed a beta hemolytic streptococcus. The temperature, which was 103 F (39 C) on admission of the patient, returned to normal in less than two days. Additional treatments were used with a humidified tent; fortified procaine penicillin G, 1 million units by intramuscular injection every four hours; and streptomycin, 0.25 Gm. by intramuscular injection every eight hours. The tracheal cannula was removed on the sixth day, and the patient went home on the eighth day.

Comment.—Some physicians fear tracheotomy because they have seen fatalities follow it; hence they tend to procrastinate and thereby seriously jeopardize the life of the patient. In my experience there are only two causes of death after tracheotomy. These can be entirely avoided if the correct diagnosis is made and proper treatment promptly instituted. The two causes are pneumothorax and crusting in the trachea and bronchi. Both conditions are correctible if diagnosis is made early.

Crusting in the trachea is too often the result of overzealous use of the aspirating catheter introduced through the tracheal cannula. To prevent destruction of the ciliated epithelium of the trachea by the aspirating catheter, I put a collar of adhesive tape around the catheter in such a position that the tip cannot be introduced deeper than 0.25 in. below the lower end of the tracheal cannula. Crusts that occasionally form despite use of a humidified tent can be loosened by dropping 5 to 15 cc. of Ringer's solution in the cannula and then placing the child in a head-low position. Further information is given by Galloway.[15]

Pneumothorax sometimes develops spontaneously before tracheotomy and sometimes is the result of injury to the dome of the pleura during tracheotomy. In either event, if the pneumothorax is promptly recognized and air is aspirated from the pleural space there will be no fatality. The following case report illustrates this type of complication.

Case 3.—A 3-year-old boy was admitted on the pediatric service with a chief complaint of croup. Symptoms had been present for only 24 hours prior to admission. Six hours prior to admission the difficulty in breathing became severe. On admission the temperature was 99.6 F (37.5 C); the respiratory rate was 40 and the pulse rate 120 per minute. Thirty minutes after admission the child became cyanotic. An emergency tracheotomy was performed without previous insertion of a bronchoscope. A no. 2 tracheal cannula was inserted without difficulty, but the child still had a pale ashen gray type of cyanosis and labored breathing. Breath sounds were absent over the left side of the chest. Thoracentesis was immediately performed, and 200 cc. of air was aspirated. The breathing and color promptly improved. It is probable that the pneumothorax was present before tracheotomy and was the cause of the sudden attack of cyanosis which prompted the tracheotomy. His convalescence was uneventful.

Comment.—If one is uncertain about the presence of pneumothorax or mediastinal emphysema, one should request prompt roentgenographic examination. Orton [16] always made it a rule to request roentgenographic examination immediately after every tracheotomy.

One of the most important recent advances in treatment has been the use of steroids. During 1958 we had 13 cases of acute subglottic laryngitis in our hospital. Medical treatment resulted in the avoiding of tracheotomy in all 13 cases. Two of these patients were given hydrocortisone intravenously and three were given prednisone, 5 mg. by mouth every eight hours. In addition, one patient with supraglottic laryngitis was given hydrocortisone intravenously, in addition to penicillin and streptomycin intramuscularly. All six of these patients had a spectacular improvement in the airway and marked reduction in the temperature within 12 to 24 hours. The following case report illustrates the value of hydrocortisone given intravenously.

Case 4.—A 6-year-old boy had fever for five days and cough and marked difficulty in breathing for 12 hours prior to admission. His temperature was

104 F (40 C); his pulse was 160 and respiration rate 60 per minute. There was marked retraction of the soft tissues above the clavicles and in the epigastrium during inspiration. Mirror examination showed marked redness and swelling of the lateral walls of the conus elasticus, so the airway was a slit only 2 mm. wide. The obvious diagnosis was severe acute subglottic laryngitis. The treatment used was therapy with hydrocortisone, 100 mg. in 1,000 cc. of 5% dextrose solution, by intravenous drip over an eight-hour period; a humidified tent; and penicillin and streptomycin given intramuscularly. In 12 hours the temperature was 98 F (36.7 C), the pulse 110, and the respiratory rate 24 per minute. The culture showed a beta hemolytic streptococcus. This child was known to have seasonal allergic rhinitis. I have never before seen such rapid improvement in a child with severe acute subglottic laryngitis.

Data on 140 Patients with Acute Laryngotracheobronchitis During Fourteen-Year Period

Year	Cases, No.	Tracheotomies, No.
1942	8	2
1943	8	5
1944	14	4
1945	13	4
1946	8	0
1947	6	0
1948*	9	2
1949	8	1
1950	17	2
1951	10	1
1952	1	0
1953	3	2
1954	3	0
1955	5	2
1956	4	1
1957	10	2
1958	13	0
	140	28

* One death occurred in 1948; no deaths in other years.

Comment.—Infections in allergic persons are usually characterized by rapid onset, violent course, and slow regression. The use of steroids quickly reduces the submucosal edema in both supraglottic and subglottic laryngitis.

The low mortality in this series of patients (see table) having acute laryngotracheobronchitis (subglottic laryngitis) is attributed to careful personal attention to each patient, large intramuscularly given doses of penicillin (3 to 5 million units daily), safe intramuscularly given doses of streptomycin (20 mg. per pound of body weight per day), cool (72 F) moist air, early tracheotomy, avoidance of catheter trauma to the mucous membrane of the trachea, and postural irrigation[15] with saline solution.

Foreign Bodies in Larynx or Upper Part of Trachea

In these cases the severity of the obstruction will depend on the size of the object and the traumatic or infectious edema which develops subsequently. If roentgenographic examination does not give a clear-cut answer to the presence or absence of foreign body, direct laryngoscopy and tracheoscopy should be done promptly to remove the object or to make certain that one is not dealing with a purely infectious type of obstruction.

The presence of a foreign body in the trachea should always be considered when one sees a dyspneic child. A wheeze heard at the open mouth is usually present in such cases.

Summary and Conclusions

Prompt differential diagnosis, followed by modern methods of treatment, will prevent death in nearly every case of acute laryngeal obstruction in children. Acute supraglottic laryngitis may require tracheotomy within four hours of the onset of the first symptom. Tracheotomy after introduction of a bronchoscope is the treatment of choice when obstruction is marked.

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PERIPHERAL NEUROPATHY AFTER EXPOSURE TO AN ESTER OF DICHLOROPHENOXYACETIC ACID

Norman P. Goldstein, M.D., Peter H. Jones, M.R.C.S., L.R.C.P.
and
Joe R. Brown, M.D., Rochester, Minn.

Severe sensory and motor symptoms necessitated hospitalization of three patients, a 52-year-old man, a 50-year-old woman, and a 65-year-old man. In each case the disorder began some hours after the use of preparations of dichlorophenoxyacetic acid (2,4-D) to kill weeds; the symptoms progressed through a period of days until pain, paresthesias, and paralysis were severe. Disability was protracted, and recovery was incomplete even after the lapse of years. There was little doubt that the neurological damage was done by the percutaneous absorption of spilled 2,4-D. The electromyographic examination supported the diagnosis of peripheral neuropathy. Since there is no antidote or other specific treatment for 2,4-D poisoning, this herbicide should be used with caution.

Disease of the peripheral nerves has been shown in the past to follow exposure to various heavy metals, organic solvents, and medicaments.[1] These substances are often used in industry and in the practice of medicine. With the synthesis of new compounds for both industrial and clinical use, it is likely that additional compounds will be shown to produce disease of the peripheral nervous system.

In three cases of polyneuritis the history indicated that exposure to the herbicide dichlorophenoxyacetic acid (2,4-D) preceded the development of the neuritis. The time relationship was such that it seemed reasonable that the herbicide caused the neurological disease.

Report of Cases

Case 1.—A 52-year-old farmer registered at the Mayo Clinic on Oct. 10, 1955, with the chief complaints of weakness, paresthesia, and aching in all four extremities. Five months prior to our examination, he had spilled about 2 fl. oz. (60 cc.) of a 10% solution of an ester of 2,4-D on his forearms. He had failed to wash it off, and that evening he had felt unduly fatigued. A few days later, nausea and vomiting had developed. These symptoms had lasted for 10 days, and during this time the patient had lost 20 lb. (9.1 kg.) in body weight.

About two months later, while again using the same concentration of this herbicide, the patient accidentally had wetted his legs with it. Over the next five days nausea and vomiting had developed and also diarrhea. A week after this second exposure to the herbicide, the patient had noted numbness and aching in the fingers and toes of both right and left extremities. He had been hospitalized. The sensations of numbness and aching gradually had extended proximally from the fingers to involve the hands, and in the lower extremities they had reached the lower part of the thighs. During the next four weeks, the fingers and toes had become more numb, and shooting pains had developed in both feet, the right foot being more painful than the left. The pain had been severe enough to require the use of narcotics. In addition, there had been desquamation of the skin of the palms and soles.

Approximately six weeks after the second exposure to 2,4-D, the condition had progressed so far that the patient was unable to walk because of the pain and weakness in both legs. He had lost sensation in both intestine and bladder but was able to urinate and control his bowel movements. An examination of cerebrospinal fluid was said to have shown an increased concentration of protein.

At the time of his admission to the Mayo Clinic, the findings on the patient's general examination were satisfactory. The neurological examination disclosed the presence of a flaccid quadriparesis that was more severe in the lower extremities. There was a sensory deficit of the hands and forearms, with moderate impairment in perception of pain, light touch, and temperature. In the lower extremities there was a similar sensory disturbance from the mid-thigh downward. Joint sensation in the fingers and toes was absent, as was appreciation of vibratory stimulation at the ankles. The muscle stretch reflexes were absent. Testing for the Babinski sign elicited no response on either side.

The hemoglobin concentration, leukocyte count, and erythrocyte count, the results from urinalysis, and the serologic test for syphilis were normal, as was the result from a sulfobromophthalein (Brom-

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From the Section of Neurology, Mayo Clinic and Mayo Foundation. Dr. Jones is a Fellow in Neurosurgery, Mayo Foundation. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

sulphalein) test of liver function. Examinations of the urine for porphyrins and for arsenic disclosed none; the lead concentration per liter of urine measured 0.03 mg.

This patient returned for reexamination on Sept. 18, 1957, stating that his condition had improved gradually in the two intervening years. By January, 1956, he had progressed sufficiently to be able to walk with the aid of crutches. In the spring of 1956 he had returned to part-time farm work. Approximately one year later he had been doing full-time work on the farm "except for heavy lifting." His complaints in September, 1957, included (1) "numbness" of the feet and fingers, (2) inability to move his toes, and (3) aching of the feet.

The neurological examination revealed marked improvement. The patient had only slight difficulty in walking on his toes and heels, although he was unable to hop on either foot. The muscle stretch reflexes were slightly hypoactive in the upper extremities; the quadriceps reflex was moderately decreased bilaterally, and the ankle reflexes were absent. Muscular strength was normal, except for slight weakness of the muscles of the lower parts of the legs and inability to move the toes. Findings on the sensory examination were normal, except for subjective hypesthesia and hypalgesia of the feet; joint sensation was normal in the feet, but vibratory sensation was moderately diminished at the ankles. An electromyogram showed only minimal denervation in the right gastrocnemius and decreased motor unit activity in the left extensor digitorum longus.

The patient wrote to us on Oct. 30, 1958, informing us that his legs had become stronger, although he still could not move his toes, and that the paresthesia of his feet and fingers had lessened.

Case 2.—A 50-year-old bookkeeper and housewife registered at the Mayo Clinic in October, 1955, with the chief complaints of weakness and numbness of both legs. She had been well until the spring of 1954. Just prior to the onset of her illness she had sprayed dandelions with a solution of an ester of 2,4-D, kneeling on the ground to do so. In the process her hands and legs had become wet with the herbicide. Shortly after this, she had noted swelling and aching of her feet and legs that had persisted for about two and one-half weeks. Rest in bed had given complete relief. The patient had been well from then until May, 1955, when after a similar exposure to the herbicide similar symptoms had occurred. She had continued to work, and the swelling had progressed to involve the knees. Her legs had not changed color, but they had felt warm.

The patient had been hospitalized for one week for observation. On the night of her discharge from the hospital excruciating pains had developed in her legs and a painful swelling in the metacarpal joints of both hands, necessitating rehospitalization that same night. While in the hospital she had been affected considerably by anorexia and had lost 20 lb. (9.1 kg.) in body weight. No fever or jaundice had been noted.

Therapy with cortisone had been started but was discontinued when the patient became agitated and depressed and had frequent crying spells. After three weeks she had returned home but had been unable to walk.

In August, 1955, there had been an episode of diarrhea of unexplained origin. After admission to a hospital for physical therapy, she had noted a rash in the groin that had spread to the thighs. The rash had itched, and a few bullae filled with serous fluid had developed. After the beginning of physiotherapy the numbness of the extremities had lessened gradually, but stiffness of the legs and difficulty in walking had persisted.

At the Mayo Clinic, the findings on the general medical examination were normal. The neurological examination revealed a flaccid paraparesis, with marked weakness of the lower part of the legs. Sensory tests of touch, pain, and temperature disclosed a moderately severe sensory deficit. The sensory loss was more marked in the feet than in the legs. In the upper extremities were a sensory loss corresponding to the ulnar nerve distribution in the left hand, and a weakness of the intrinsic muscles of both hands. The Achilles reflexes were absent, but the other tendon reflexes were not unusual.

The hemoglobin level and the erythrocyte and leukocyte counts were normal. Albuminuria, with albumin content of grade 2, was the only unusual finding in urinalysis. The result of the serologic test for syphilis was negative. The fasting blood sugar level was normal. Findings from tests for lead, arsenic, and porphyrins in the urine were negative.

An electromyographic study showed denervation in several peripheral muscles, with typical fibrillation potentials. The proportion of polyphasic motor unit potentials was above normal. The velocity of conduction was slower than normal in the left ulnar nerve (37 meters per second).

On Nov. 21, 1958, we received information about this patient from her family physician. She had improved, although she still had some pain in the legs. She was able to walk but was clumsy on her feet. The paresthesia also had lessened. She was able to do her own housework, despite the fact that she had fallen and fractured one arm. In general, she was considered to be approximately two-thirds recovered from her worst stage in 1955.

Case 3.—A 65-year-old farmer registered at the Mayo Clinic on Oct. 13, 1955, with the chief complaint that pain in the lower extremities and twitching of muscles had persisted for five months. Prior to the onset of this complaint, he had spent two *days spraying a cornfield with a solution of an* ester of 2,4-D. During this time his sleeves and trouser legs had been wetted with the herbicide. On the next day increasing malaise, headache, nausea, and finally vomiting had made him retire early. On the following day vertigo had prevented his standing, and vomiting had been frequent. After four or five days he had felt generally improved, but at this time he had noted paresthesia of the extremities and pain in the legs, as well as twitching of the muscles of the calves and arms. He described the paresthesia and muscle twitching as a "feeling of worms crawling beneath the skin." Gradually the fasciculations had become more pronounced, until all skeletal muscles were involved. No muscular weakness had been noted.

General examination revealed old healed pulmonary tuberculosis, chronic glomerulonephritis, and atrophy of the right testis. The blood pressure was 120 mm. Hg systolic and 80 mm. Hg diastolic. Neurological examination revealed generalized, extensive fasciculations that were fine to coarse. No objective sensory or motor deficit was found. No evidence of disturbance of the autonomic nervous system was noted. Funduscopic examination disclosed minimal changes of hypertensive sclerosis.

The concentration of hemoglobin and the counts of erythrocytes and leukocytes were within normal limits. The sedimentation rate was 41 mm. in one hour (Westergren method), and the blood urea level 40 mg. per 100 ml. In the urine no arsenic and only 0.04 mg. of lead per liter were found. Urinalysis showed persistent albuminuria and occasional casts. On examination of the cerebrospinal fluid, the findings from manometric studies were normal, as was the appearance. The concentration of protein was 65 mg. per 100 ml., one lymphocyte was present, the Wassermann reaction was negative, and the colloidal gold curve was 0000000000.

An electromyogram (made by Dr. E. H. Lambert) showed no evidence of denervation. The velocity of conduction of the left peroneal nerve was slightly slowed (38 meters per second). Motor unit potentials were normal. Fasciculations were of the grouped discharge type and similar to those that can be caused by drugs such as neostigmine.

This patient returned for reexamination on Aug. 24, 1956. He stated that he had constant pain in the upper and lower extremities. He had stopped working in November, 1955, because of the pain. The fasciculations had persisted. Prednisone therapy for three months had not lessened the pain or fasciculations, and he was taking codeine to control the pain. Minimal paresthesia was present in all four extremities.

The findings from neurological examination were essentially unchanged, except for a slight decrease in perception of vibratory stimuli at the ankles. An electromyographic examination indicated no significant change from the status disclosed by the *previous examination.*

Comment

In all three of the cases reported above, symptoms and signs of a general toxic reaction as well as involvement of the peripheral nervous system developed after exposure to an ester of 2,4-D. So far as we know, there have been no other reports of a toxic reaction to this substance in humans. Hildebrand[2] mentioned that some investigators consumed unreported amounts of 2,4-D and suffered no ill-effect. He also stated that the 2,4-D solution is not irritating to the skin.

Hill and Carlisle,[3] however, in autopsies on animals subjected to chronic poisoning, found renal edema with tubular changes; in some dogs they also found evidence of damage to the liver. Bucher[4] noted the production of temporary myotonia in several species of laboratory animals after a single injection of 2,4-D. He did not find any striking change on histological examination of various organs, but he did note that parenteral administration in dogs caused sneezing, lacrimation, and rubbing of the eyes, as well as a gastrointestinal disturbance with vomiting and anorexia. In mice, besides the myotonia and other reactions found in dogs, there were diarrhea, sluggishness, reluctance to move, rigidity of the tail; and a coarse clonic tremor. Coma and death followed in some animals, while others recovered without residual neurological deficits.

Sollmann[5] has said that a syndrome of myotonia, stiffness of the extremities, ataxia, lethargy, paralysis, and coma may follow the parenteral administration of 2,4-D in experimental animals. Large doses ~~may cause~~ ventricular fibrillation also.

In plants, a concentration of 10 ppm of 2,4-D stimulates growth. When the concentration is increased to between 100 and 1,000 ppm, the excessive stimulation of growth kills the deep root system.[5] It has been postulated that the metabolism of phosphate is interrupted or inhibited.

In our patients the toxic substance entered through the skin and possibly also by way of the respiratory system. The 2,4-D had been diluted, but still, with wetting of the extremities and the clothing, the exposure apparently was greater than usual. The involvement of the peripheral nervous system could be a result of a direct toxic effect, or possibly a sensitivity reaction, such as that seen after the injection of a vaccine or an antitoxin. At present, the mechanism of toxicity that follows exposure of mammals to 2,4-D is not known.

In order to prevent further cases of neuropathy from this herbicide, it seems logical to recommend shorter periods of exposure, frequent washing of the skin, and changing of clothes when they become wet with the solution. No antidote is known, and there seems to be no specific treatment for the neuropathy if it develops.

Summary

Three cases of polyneuritis occurred after heavy exposure to an ester of dichlorophenoxyacetic acid (2,4-D). The mechanism of the toxicity affecting the peripheral nervous system is unknown. There is no antidote and no specific treatment.

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THE PROCTOLOGIST AND THE PRACTICE OF MEDICINE

A. W. Martin Marino, M.D., Brooklyn, N. Y.

There is evidence that proctology was practiced in ancient times and existed even then as a specialty. Nevertheless a proctologist should be a physician first and a specialist second. There are many conditions, such as pruritus ani and hemorrhoids, that should not be treated locally until there has been a general search for causative factors. Conversely there are many conditions that should not be treated systemically until the physical examination has included a proctologic survey for the diagnostic information it may yield. Specialties rise as their need arises and fall for lack of usefulness. Proctology is a much-needed specialty, but physicians must never forget that, whatever their regions of special interest, they are treating human beings and not just diseased parts of people.

While ours is called the "age of specialization," a look back through the centuries reveals that specialization had developed to a marked degree in the earliest times of which there is any record. Imhotep, an Egyptian of the third dynasty (about 3000 B. C.), the earliest known physician, was especially skilled in relieving pain by producing sleep. Herodotus of Halicarnassus, the Greek historian, reporting his travels in Egypt in the fifth century B. C., recorded the following statement (same meaning given by various translations):

> The art of medicine in Egypt is thus exercised: each physician is confined to the study and management of one disease only; there are of course a great number who practice this art; some attend the disorders of the eyes, others to those of the head, some take care of the teeth, others are conversant with all diseases of the bowels; whilst many attend to the cure of maladies which are less conspicuous.

As a general rule, however, practitioners who were especially skilled in a branch of medicine in ancient times were not necessarily "full specialists" as we define specialists today. They were apt to be men who were more proficient in one phase of practice and devoted more time to that phase in the course of their general practices.

Pioneers in Endoscopy

The means to inspect adequately and to explore visually the hollow viscera, such as the urinary bladder, trachea and bronchi, esophagus, and the large intestine, for diagnostic and therapeutic purposes, was made possible by ingenious men of vision with inquiring minds. The urologists were the pioneers in such work. It was Philip Bozini who in 1805 devised the first endoscope, which he called the *lichtleiter*, an illuminating tube with which to see inside the urinary bladder.

It was not until 1895 that the first proctoscope and sigmoidoscope were introduced, and it remained for Howard Atwood Kelly of Johns Hop-

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From the Department of Surgery, Division of Proctology, the Brooklyn Hospital, and the Department of Surgery, State University of New York Downstate Medical Center, College of Medicine.

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kins to do so. The proctoscope was 6 in. in length and the sigmoidoscope 8 in. long. Illumination was obtained by means of reflected light with a head mirror. Hermann Strauss of Berlin in 1910 improved Kelly's endoscope by adding an inflating device. Up to that time the distending effect of atmospheric air was depended on to help balloon out the rectum. It was not long before very practical electrically lighted proctoscopes and sigmoidoscopes became available. The lighting has been improved to the degree that instruments 12 in. in length and longer can be introduced through the anus in suitable patients for exploration of the sigmoid and rectum. Modern proctoscopes are 8 to 10 in. long, and sigmoidoscopes are 10 to 12 in. long. There are instruments that can reach higher in selected patients, but these instruments are not practical for ordinary use. In his "Traite' D'Endoscopie," in 1926, Bensaude makes the following statement:

> Rectocolic endoscopy such as we practice today in Europe, is entirely due to the work of American authors, and the outcome of this mode of exploration, inaugurated by Desormeaux, may be compared to that of intubation, which born in France with Bouchut's investigations, was completely forgotten there until the day it came back from America with the instruments perfected by O'Dwyer.

Earliest Records of Proctologic Disorders

Wide prevalence of diseases of the colon, rectum, and anus was recorded in the earliest writings with which we are acquainted. In the Code of Hammurabi (about 2200 B. C.) is found the following statement: "If a doctor . . . has cured the diseased bowel, the patient shall give five shekels of silver to the doctor." Eber's papyrus from Egypt (about 1550 B. C.) alludes to hemorrhoids. The Hindus (about 1000 B. C.) had knowledge of hemorrhoids and five kinds of anal fistulas. In the Old Testament there are references to proctologic diseases.

We are on firmer ground with the Greek writers (about 400 B. C.), for in addition to their manuscripts some of the instruments actually used in the treatment of rectal disorders have been passed on to us. The diagnosis and treatment for anorectal fistulas is discussed in the Hippocratic writings. Celsus (first century A. D.), in his encyclopedic work, discussed the diagnosis and treatment of fistulas. Galen, who flourished in 165 A. D., had a theory that ascites could be caused by blood retained in hemorrhoids. Nothing further of importance to record can be found until the sixth century, when Aetius, physician to the Court of Constantinople, advised the actual cautery for procidentia recti, a procedure which under certain circumstances is still in use.

We now skip to the 14th century to the time of John Arderne, whose treatise on the cure of fistula embodied some major principles which still hold. Now, another skip to 1819, at which time a set of iron and bronze surgical instruments were unearthed in the long-buried city of Pompeii. Among them is a two-bladed speculum for anal and rectal examinations, a modification of which has its modern counterpart. The year 1835 is a memorable one in the history of proctology, for it was the year that Frederick Salmon of London founded St. Mark's Hospital for Fistula and Other Diseases of the Rectum. Later, also in London, the Gordon Hospital for Diseases of the Rectum was erected.

Early American Proctology

Joseph McDowell Mathews of Louisville, Ky., the 51st president of the American Medical Association, is referred to as the father of American proctology. Seventy-five years have elapsed since his decision to limit his practice to proctologic disorders, and he prepared himself for the specialty by visiting clinics and medical centers in New York and London. He spent considerable time at St. Mark's Hospital with the Allinghams and others.

After his return to the United States, after some cursory attempts, a meeting was called in 1899, largely through his efforts, for the purpose of organizing a society for those interested in this special branch of medicine. In that year and from that meeting the American Proctologic Society was founded. Mathews was its first presiding officer. Since then the Society has fluorished.

After four years of preliminaries, finally, in 1916, a Section on Proctology of the American Medical Association was organized and combined with the Section on Gastroenterology. The first session of the Section on Gastroenterology and Proctology of the American Medical Association was held in New York City in 1917, 42 years ago. These special fields of medicine have progressively developed through the untiring endeavors and zeal of its devoted leaders to whom the Section owes its success.

The proctologist or, if another name is preferred, the specialist in the diagnosis and treatment of colonic and anorectal diseases is a bipartite specialist, having both medical and surgical methods available, and for that reason is in an advantageous position to treat conditions such as chronic ulcerative colitis and decide promptly when medical treatment should be discontinued and surgery instituted, rather than permitting the disease to progress to a state of inoperability.

Actually some form of proctology is practiced by specialists in other fields, as well as by general practitioners. I am certain that recognized roentgenologists and dermatologists do not treat pruritus ani until and unless the causative factor or factors have been searched for, but there are persons whose office equipment includes x-ray machines who will treat that condition by radiation without the benefit of proper proctologic examination.

As a proctologist I have found it profitable to attend selected sessions of the Sections on Anesthesiology, Dermatology, General and Abdominal Surgery, Pathology and Physiology, and Radiology of the Scientific Assemblies of the American Medical Association, as well as those of my state medical society. The truth of the matter is that, although specialists practice a limited branch of medicine, they do and should have overlapping knowledge of other departments of medicine. Disorders such as perianal melanoma, epidermoid (squamous cell) anal and perianal carcinoma, perianal warts, and allergic and fungoid conditions demand an interrelationship and interchange of information and ideas.

Physician First—Specialist Second

We should be physicians first and specialists second. There is a natural interrelationship among several specialties, and this relationship should be accepted amicably and with cooperation and not decried. I submit that pruritus ani not infrequently deserves and receives the benefit of dermatological, medical, and roentgenologic consultations, but no such case should be treated unless a proctologic survey has been completed.

Because of the proximity of pilonidal disease to the anus, proctologists treat that condition, though it has no embryologic connection with the intestine. Perhaps it belongs in the realm of general or even orthopedic surgery, but advances reported in the treatment of pilonidal disease have emanated principally from proctologists who have devoted considerable study to the subject.

Proctologists are exposed to many incidences of regrettable complications due to inexpert therapy, and calling attention to such occurrences should not be cause for taking umbrage. Of course it may be stated that the proctologist sees only the poor results, but there should not be as many avoidable poor results as come to our attention. I hasten to emphasize that general surgeons properly trained in colonic surgery do excellent work in that category. But the modern proctologist emerges only after having had the [illegible] general, including a good measure of colonic, surgical training as well as specialized training in anorectal surgery, and he is a source of good proctologic practice for the community in which he chooses to locate. Wherever proctology is not practiced as a specialty, anorectal diseases and many aspects of colonic disorders assume a lesser position and often do not receive proper consideration and attention.

General surgeons or surgical specialists, including proctologists, may choose to perform some operations and not others. There are not now many surgeons who demand all surgery for their domain. Wherever such a person may exist he must be aware that in the performance of such an all-encompassing variety of operations, his effectiveness must be deficient and below standard in some fields.

As medicine advances and certain diseases are conquered, the need for a specialty may be obviated, or modification and revision of a specialty may become necessary. The introduction of revealing research findings may alter the entire conception and method of procedure toward a medical or surgical problem and thereby markedly affect a specialty. The discoveries in the modern treatment of tuberculosis, and the modern use of sulfonamides and antibiotics, are examples of the change that can be brought about by new findings. Specialties rise as their need arises and fall for lack of usefulness. But unless the practitioner is a "one disease specialist," specialization will continue to occupy a useful and necessary place in the practice of medicine.

As stated earlier, proctology means more than the treatment of hemorrhoids, fistulas, and pruritus ani. A visit to the proctologic clinic of an accredited hospital staffed by men who are well trained, expert, and dextrous will make the visitor realize that proctology is a much needed specialty. Only those unfamiliar with the activities in modern proctologic clinics believe differently. Many of our medical schools, recognizing the need for adequate proctologic instruction, have established divisions or departments of proctology, but there are some which style themselves great medical centers where only meager attention is paid to the teaching of proctology. Graduates of such schools become very conscious of what they missed in school when as interns they are given proctologic instruction.

Duties and Responsibilities

We of the medical profession, whether specialists or general practitioners, have a duty and responsibility to the individual men and women and their children who come or are brought to us in their time of need and anxiety. We should give attention to the personal and emotional requirements of these persons, as well as the scientific medical care which they seek. As physicians we must never forget that, whatever the region of our special interest, we are treating a person and not just a diseased part of that human being. We who are privileged to share the confidences of our patients must practice the art as well as the science of medicine and thus be of the most possible use to those who place their lives and trust in our hands. This can be done and is being done through the wholehearted collaboration between specialists and generalists who complement each other's efforts toward the promotion of the health and well-being of our fellow man.

80 Hanson Place (17).

INCOMPETENT OS OF THE CERVIX AS A CAUSE OF FETAL LOSS

E. Stewart Taylor, M.D.
and
Richard R. Hansen, M.D., Denver

The surgical procedure here described aims to prevent premature birth and fetal wastage caused by weakness of the musculature of the cervix uteri. The operation, devised by Shirodkar, consists of the application of a purse string or tourniquet to the cervix. It is indicated only for patients who have a history of repeated unexplained miscarriages during the second trimester and who demonstrate a progressive cervical effacement and dilatation between the 14th and 28th weeks of gestation. It was performed in 40 patients who had had 182 previous pregnancies with 20 premature and only 15 full-term infants surviving. Among the 40 patients after operation, only 8 had unsatisfactory results, for reasons here analyzed, while 32 delivered normal infants, including two sets of twins. Ten deliveries occurred per vaginam after removal of the purse string, and 22 were cesarean.

The incompetent internal os of the uterine cervix has been found to be a cause of premature termination of pregnancy between the 16th and 28th weeks of gestation. This condition occurs no more than once in 500 pregnancies, according to our experience at the Colorado General Hospital. We have, however, been able to collect data on 40 patients who have been surgically treated for an incompetent internal cervical os. The treatment was carried out during pregnancy in each instance. These patients and their management are the subject of this report. The patients in this group have been under the care of members of the department of obstetrics and gynecology and have been operated on in the past two years at Colorado General Hospital, Denver General Hospital, Fitzsimons Army Hospital, and private hospitals of this community. The operative procedure used is a modification of an operation originally suggested by Shirodkar[1] of India and introduced to the United States by Barter and associates.[2] In principle, the operation consists of a purse-string suture placed submucosally around the cervix at the level of the internal os in order to prevent expulsion of the fetus before maturity.

Lash,[3] in 1949, was the first person in the United States to focus attention on the incompetent cervix as a cause of abortion. He stated that the incompetent cervix was a result of trauma and that a defect could be found in the cervix. Since then the diagnosis of incompetent cervix has been made in women without a history of cervical trauma and without a recognized physical defect of the cervix. Palmer[4] postulated the congenital incompetent cervix and described a short weak cervix; he called the condition "hypoplasia of the cervix." Jeffcoate and Wilson[5] performed hysterographic studies on selected women whose obstetric histories were unknown to the radiologist. Of 31 women who had experienced normal labors at term, one had a funnel cervix and 5 had minor cornual malformations. Of 69 women who had experienced premature labor of unknown cause, 33 had a dilated internal os and 15 had cornual malformations. Barter and others[2] suggest erect posture of man as a factor in congenital incompetence. Baden[6] has discussed the physiological relative cervical incompetence in twin gestation.

Diagnosis

The diagnosis of the incompetent cervix is suspected through history of recurrent middle trimester fetal losses. There is usually a sudden painless passage of amniotic fluid between the 16th and 28th weeks of gestation followed by almost immediate expulsion of the conceptus.

In one-half of our patients, there was a history of previous gynecologic or obstetric trauma. Trauma may arise from a previous delivery, instrumental dilatation of the cervix, hysterotomy, or cervical amputation. A midforceps operation or a difficult breech extraction may cause damage to a cervix, with later incompetence. An apparently normal term delivery may rarely destroy the functional integrity of the cervix. A visible cervical laceration may cause cervical incompetence in subsequent pregnancies.

Presumptive evidence of cervical incompetence can be demonstrated by the painless passage of a 7-mm. Hegar dilator through the internal os of the cervix while the patient is not pregnant. Uterine anomalies such as a bicornuate uterus must be considered in the differential diagnosis of repeated abortions. Hysterographic confirmation of cervical incompetence is not necessary, but a hysterogram is valuable for the demonstration of abnormalities of the uterine body.

An important clinical test for the presumed incompetent cervix is careful observation of the cervix during pregnancy. The patient who has an incompetent cervix will demonstrate cervical effacement

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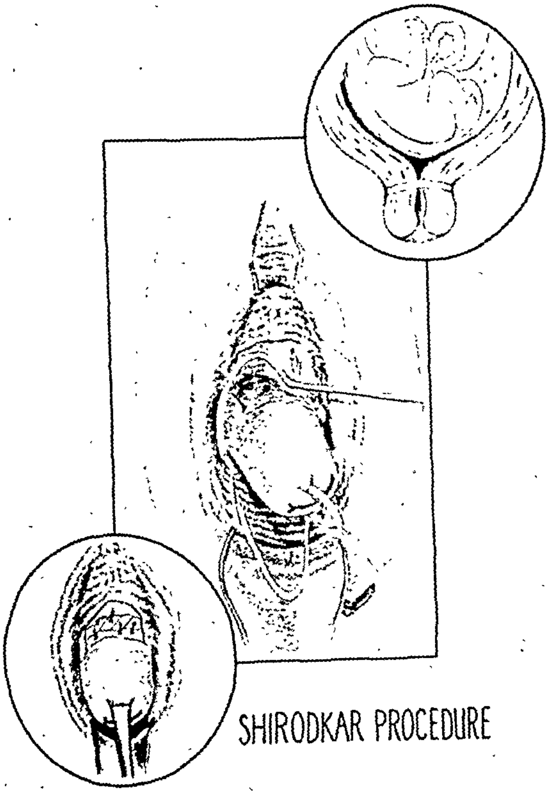
From the Department of Obstetrics and Gynecology, University of Colorado Medical Center.

and dilatation starting between the 14th and 20th weeks of gestation. A suspected diagnosis is confirmed when the cervix begins to dilate and membranes can be observed or palpated in the cervical canal. The open cervix should be detected before the membranes prolapse into the vaginal vault. If prolapse of the membranes occurs, the intrauterine volume diminishes, with possible shearing of the placental bed, bleeding, and delivery of the immature fetus. In other instances, the exposed membranes become infected and rupture, and delivery occurs soon thereafter.

Treatment

Treatment of the incompetent cervix depends on the cause. If there is a history of previous midtrimester fetal loss, and a deep laceration of the cervical canal, this defect should be repaired by trachelorrhaphy when the patient is not pregnant. Any other procedure in these patients is likely to fail because the basic defect is not corrected. Two of our failures demonstrate the improper selection of operative procedures for the incompetent cervix. A purse-string suture around the internal os is not proper treatment for cervical incompetence secondary to a laceration of the cervix.



Principles of Shirodkar procedure to correct incompetent internal os of cervix during pregnancy.

Shirodkar[1] has emphasized his observation that bed rest will often avert the premature labor in this syndrome. He sought a more certain method of reinforcement of the cervix. Shirodkar used a fascia lata transplant placed submucosally around the cervix as a tourniquet at the level of the internal os.

Indications and Contraindications.—The Shirodkar procedure is indicated only for patients who have a history of repeated unexplained midtrimester fetal loss and demonstrate a progressive cervical effacement and dilatation between the 14th and 28th weeks of gestation. Durfee[7] reported six consecutive failures to avert labor when a surgical procedure for closure of a partly dilated cervix was performed on patients as late as the 28th week of pregnancy.

Table 1.—*Successful Results of Treatment of the Incompetent Cervix*

	Previous Pregnancies			Cervix Closed by Operation	
Patient No.	Fetal Losses, No.	Term Deliveries, No.	Surviving Premature Infants, No.	Week of Gestation	Infant Weight, Gm.
1	7	0	0	21	2,780
2	7	0	0	26	2,420
3	1	0	3	24	2,400
4	6	0	0	15	2,740
5	2	1	0	25	2,600
6	1	0	0	18	*
7	2	0	0	19	*
8	2	0	0	21	2,640
9	5	0	0	18	2,700
10	5	1	1	18	3,240
11	5	0	0	15	2,770
12	4	0	1	16	3,100
13	1	1	3	23	3,040
14	5	0	0	20	2,880
15	6	0	0	14	2,760
16	2	0	0	20	2,580
17	3	0	0	16	3,200
18	4	1	4	30	1,900
19	2	0	0	25	3,400
20	2	2	3	27	4,000
21	3	1	0	22	3,480
22	5	0	1	22	2,000
23	1	0	0	20	1,900
24	3	4	0	23	3,400
25	5	0	0	23	3,400
26	3	0	0	16	3,060
27	3	1	0	12	2,650
28	2	0	2	16	3,280
29	3	1	0	23	3,500
30	2	0	0	19	3,210
31	10	0	0	14	3,290
32	6	0	0	13	3,100

* Twins.

Technique of Operation.—Our technique (see figure) is similar to that described by Barter and others.[2] The patient is given a general anesthetic for the operation. The anterior and posterior lips of the cervix are grasped with separate tenacula, and a 3-cm. transverse incision of the posterior vaginal mucosa is made at the level of the internal os. A similar anterior incision is made, and the bladder is dissected free from the cervix to the level of the internal os. An 8-mm. Mercilene tourniquet is then passed around the cervix at the level of the internal os, as demonstrated in the illustrations. This band is then tied as tightly as possible. Anchoring sutures of silk are then placed through the band and cervical fascia, anteriorly and posteriorly. The vaginal mucosa is closed with interrupted chromic catgut sutures.

The postoperative course is usually uncomplicated. The patient is able to leave the hospital on the fourth or fifth postoperative day. No progesterone or other hormone treatment is used. The patient should be cautioned to abstain from intercourse for three weeks. Normal household activities may be resumed one week after the operation.

Results

Our group of 40 patients had had 182 previous pregnancies with only 35 surviving infants, a reproductive efficiency of 19% (tables 1 and 2). More important is the fact that only 15 of the 35 surviving infants were at term when delivered. The term deliveries occurred as the first pregnancies experienced by these patients. A normal term delivery, therefore, seems to be followed by cervical incompetence in a rare instance. The other 20 surviving infants were born prematurely. Seven of these infants have permanent complications of prematurity, such as blindness and mental retardation.

TABLE 2.—*Failures in Treatment of the Incompetent Cervix*

Patient No.	Week of Gestation at Operation	Week of Abortion	Apparent Cause of Failure
33	16	21	Deep cervical laceration with protrusion of membranes; spontaneous rupture of membranes
34	22	22	Deep cervical laceration with protrusion of membranes; intrauterine fetal death
35	19	23	Abruptio placentae
36	26	27	Ruptured marginal sinus of placenta and delivery
37	25	27	Tourniquet slipped
38	14	22	Prolapsed membranes, intrauterine death
39	16	16	Spontaneous rupture of membranes
40	14	17	Spontaneous rupture of membranes

Thirty-two of the 40 patients who have had a Shirodkar operation performed during pregnancy have been delivered of normal infants. Our success rate is 80%. There has not been a failure in the last 16 operations performed. Two sets of twins were born to the successfully treated group. Twenty-two of the successful group were delivered by cesarean section, while 10 delivered vaginally after removal of the tourniquet.

There were eight failures in our series of 40 patients who were treated surgically during pregnancy after a diagnosis of cervical incompetence had been made (table 2). Two patients should not have had a band placed around their cervices because they had deep lacerations of the cervix that needed trachelorrhaphy. These patients have each since had a trachelorrhaphy. In two other instances, the cervix had been dilated widely before operation and the membranes were prolapsed through the cervix. Rupture of the membranes occurred a few days after the operation had been performed.

If a cesarean section is performed, the integrity of the cervix is conserved and future term pregnancies are probably assured. Three of our 40 patients are pregnant for the second time, and their pregnancies are progressing normally.

Comment

The type of suture material used for closure of the cervix has little effect on the final results. We have discontinued the use of homologous fascia lata transplants because of the problems secondary to obtaining fascia from the patient's thigh. We are currently using an 8-mm. single-thickness strip of Mercilene tape. Mercilene tape is strong and stimulates adequate fibrosis but causes very little other tissue reaction. It has an advantage in that the 8-mm. size cannot be tied too tightly about the cervix. The nonabsorbable tourniquet may be removed after termination of the pregnancy if abnormal tissue reaction results.

The incompetent cervical os is a positive entity for which a surgical treatment is available and effective in a high percentage of patients if the diagnosis is correct. There are certain patients who have such a prolonged history of midtrimester fetal losses that the diagnosis can be made practically by history alone. It is our opinion that the incompetent cervical os should be treated only during pregnancy, after the cervix has begun to show signs of incompetency. The patient who is suspected of having an incompetent cervical os should be examined frequently during her pregnancy for signs of early effacement and dilatation of the cervix. Dilatation of the cervix is gradual and usually is not perceptible to the examiner before the 14th week of pregnancy. It has been our experience, however, that wide dilatation of the cervix with prolapse of the membranes combine to make a poor prognosis even after operative closure of the cervix. It is necessary, therefore, to interfere with surgical closure before dilatation of the cervix has progressed beyond early dilatation if the best results are to be obtained.

Conclusions

Incompetence of the internal cervical os is an infrequent but important cause of midtrimester abortion. Surgical correction of the incompetent internal cervical os during the second trimester of pregnancy is attended by successful pregnancies in at least 80% of patients, if the patients are properly selected for operation. The operation is best performed not earlier than the 14th gestational week and not later than the 27th week. The patient suspected of having incompetency of the internal cervical os should be examined during pregnancy at weekly or biweekly intervals so that pathological and early effacement and dilatation of the cervix may be diagnosed. Surgical closure should be considered only after the internal os has started to dilate.

4200 E. Ninth St. (20) (Dr. Taylor).

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MEDICAL PRACTICE, MEDICAL CARE, AND MODERN SOCIETY

Malcolm S. M. Watts, M.D., San Francisco

Medical practice, public health, and social welfare have a common basic goal—to work for the best interest of the patient, the individual human being. This must always be clearly recognized by all concerned in their thinking and action. This goal finds its highest expression in terms of the golden rule. The *medical care provided for others must be only that which one would wish to receive for oneself.*

Problems in Providing Best Care

The problems of medical practice, medical care, and modern society bring us face to face with some of the most complex problems of our times. Perhaps some definitions are in order. First, who are those who provide this care and who are those who receive it? It is clear that the providers cannot be limited to doctors, nurses, medical technicians, health departments, and social welfare agencies. These groups do not supply the necessary funds. The providers, therefore, must also include those responsible for the source of funds, which in any scheme for medical care is ultimately the consumer or the public. In the final analysis this includes everyone. Every person must meet these costs out of his own pocket; through prepayment; by means of funds provided by industries, through increased cost of living; or directly or indirectly in taxes. It also follows that in these broad terms the recipients of medical care cannot be limited to those who are sick, injured, or maladjusted at any given moment but must include anyone who is or may become sick; this, too, includes everyone. Thus, in these social terms, those who are to provide the medical care and those who are to receive it are the same.

It is fallacious to consider medical care as a product or commodity, to assume that medicine has developed into a precise science, to think that medical care is not ultimately paid for by somebody, or to suppose that the interests of the community so nearly coincide with those of the individual person that he can be reduced to a file number without personalized care. There are many types of medical practice and many ways of financing the operation of hospitals and offices, the wages of personnel, and the costs of equipment and medicaments. The experience of the California Medical Association shows that it is possible to develop successful programs that will interfere but little with the traditional relationship between doctor and patient.

Therefore, it becomes of most practical importance to be careful to provide only that kind of medical care for others which one would wish to receive for oneself and one's family.

Just what are the essentials of this medical care which Americans, individually and collectively, must provide for themselves? A recent report[1] of a committee of the American Medical Association provides an answer. "Medical care is that service which uses every means available to secure and maintain a state of physical and mental well-being in the individual. Good quality medical care results from the full use by the physician of his art, skill and knowledge, and his utilization of the scientific facilities available to him. It depends upon the phy-

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Assistant Dean, University of California, School of Medicine; Chairman, Public Relations Committee, California Medical Association.

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sician's sincere interest in the patient and the patient's faith in his physician." Thus, the essentials include the patient's needs, the physician's desire to help, the patient's belief that the physician can and will help, and the tool or technology by which the help is given.

It is often inferred that medical care is not now provided for all who need it. To any extent that this is true, it presents a serious problem to society and to the medical profession. However, it has long been a matter of pride to the medical profession that it, with the support of the community, has always seen to it that everyone receives basic necessary medical care regardless of ability to pay and that the standards of this care are as high as anywhere in the world. It would appear rather that present problems in medical care pertain to its rapidly increasing cost and complexity; changes in the social, economic, and political environment in which it must be rendered; and the need to insure that the best medical care is available to each individual in these changing circumstances. Fundamentally, this is of supreme interest to everyone, since, in social terms, the ultimate providers and the ultimate recipients are basically the same persons.

Some Causes

What lies behind these complex problems? The phenomenal growth of science and technology, particularly in the last 50 years, has had profound effects on medical care and has increased its complexity and cost. It has led to specialization which extends even beyond the medical profession and includes the work of many paramedical technologies and many public and voluntary health and welfare agencies. Further, this growth of science and technology has affected the whole of society and has served to bring everyone into closer and more interdependent relationship.

Profound economic changes have also occurred. The devaluation of the dollar together with rising taxes during the last 25 years have made it almost impossible for the average person to save adequately to meet the modern cost of serious illness. Techniques have therefore been developed to spread this cost more evenly throughout the population. These include prepaid funds for medical care, tax-free funds in the form of "fringe" benefits, and the use of tax funds themselves. These developments have produced complex changes in so-called traditional medical practice.

There have also been important social and political trends which are probably inherent in the evolution of our democracy. Over 100 years ago de Tocqueville predicted that in a democracy based on the principle of majority rule, the particular interests of the individual person would gradually become subservient to the principle to the greatest good for the greatest number. There is considerable evidence to suggest that this is in fact now occurring. Public officials increasingly rely on the advice, counsel, and financial support of organizations representing the special interests which large groups of persons have in common. Even the courts seem less apt to uphold the right of a person to be different. In passing, it is a curious paradox that "advances" in democracy tend toward compulsory collectivism while the collectivist states themselves have rediscovered that individual persons are not all alike and have found it necessary to reward individual initiative, responsibility, and accomplishment.

What bearing do these developments have on the medical care which everyone must provide for everyone who needs it? There has been much confusion. In the smoke, fire, and emotion that has been generated it is all too often forgotten that the goal is to do what is best for the patient and that the patient is an individual human being whose medical problems may be the same or different from those of his neighbors.

Some Fallacies

Several fallacious concepts have been introduced which have had surprisingly wide acceptance and therefore bear on the problem.

1. Many persons have come to consider medical care to be simply a product or commodity consisting of diagnostic procedures, x-rays, laboratory tests, operations, pills, injections, and the like. To them, the answer to any problem in medical care lies merely in applying well-known mass production and mass distribution techniques to this commodity in the good old American tradition.

2. Others have come to believe that medical care is in fact a precise science, which could almost guarantee health for all if it could only be made available to everyone. This fallacy is also obvious. Medical science is by no means developed to this point, but even if it were precise, the patient is not, and therefore medical care can never be. This fallacy is perilously close to that of the hopeless search of Ponce de Leon for the fountain of youth.

3. Economic developments also have led to curiously unclear thinking. It is believed by many that medical care should be "free." The fallacy here is obvious. It must ultimately be paid for by the ultimate consumer—the patient. The more complex the system the more costly it becomes, because the costs of the system must be added to the costs of patient care. Also, it is often assumed the doctor will work devotedly in the interest of his patient no matter who pays him. This somehow assumes that doctors are different from other persons, and this is not true. To the extent that a union doctor works for the union, a government doctor works for the government, an insurance doctor works for the insurance company, or a doctor works for a closed panel, a group, or a clinic, his interest in the patient is proportionately reduced. As a corollary to this, when pools of money for medical care are collected through prepayment, fringe benefits, or

tax funds, the question is seldom asked "whose money is it?" Such funds are rarely handled as though they belonged to the patient. This has far-reaching implications in terms of who is working for whom, the special interests of so-called third parties who operate the funds, and the personal interests of the patient whose ailments may be no one's business but his own.

4. The principle of the greatest good for the greatest number and its development in our democracy has been mentioned. Under what circumstances does this principle apply in the best interest of the individual patient? On reflection, it would appear that it applies whenever there is, or may be, a great disparity between the numbers of persons in need of medical care and the amount of services which may be available. Thus, it has been found to apply in potentially epidemic situations such as when the public health is endangered, in military medicine, in civil defense, and also in certain remote or economically backward areas where adequate facilities and services are not available. But the principle of the greatest good for the greatest number has not been found appropriate to the best medical care for the individual patient in the normal circumstances of American life. The average American has received and continues to be entitled to personalized care for his individual needs which may or may not be similar to the problems of others. This best medical care is and should continue to be the goal and purpose. The individual human being should not be reduced to the status of a statistic or a file number and receive his medical care as a statistical probability.

5. Reference has been made to some political trends in the evolution of democracy. The fundamental question here appears to be "To what extent is 'freedom to' to be sacrificed for 'freedom from'?", i. e., "To what extent is the independence of the individual and his right to personal consideration to be sacrificed to dependence on and interdependence with the greatest good for the greatest number?" Medical care is now considered a social necessity along with food, shelter, and clothing. But so far, no one in America has seriously proposed that a person's right to choose his food, shelter, or clothing be curtailed. The community has always provided the essentials for those who were unable to afford the basic necessities. Perhaps it is as fallacious to compel a person to sacrifice his freedom to have the medical care he chooses as it is to expect him to sacrifice his freedom to choose his food, his housing, and his clothing. In this sense, medical care problems are fundamental to individual freedom in the American way of life.

If it is agreed that only the best in medical care can be satisfactory for Americans, then medical care must be personalized and individualized and the dignity of the human being maintained. Anything less is acceptable only as a stop-gap emergency measure. The patient's special and particular needs for medical care must be recognized, diagnosed, and treated by a doctor whose primary interest and obligation is the health and welfare of his individual patients. Tools and technology must be available economically and otherwise. The element of the patient's belief that the physician can and will help with his problem must be preserved. Somehow, these essentials of the best medical care must remain realities in the new technological, economic, and social environment.

The Experimental Approach

The medical profession is an old profession. It knows the meaning of truth. It knows that, if something was really true yesterday, it is true today and will still be true tomorrow. It knows that these essentials of medical care are such truths and that they must somehow be preserved in the interest of the patient if the true goal of the best medical care for all is to be achieved. In the historical development of its science and technology, medicine has dealt with many complex problems. It has tested and applied old truths in many new situations. In its research it has explored many blind alleys. It has seen many promising drugs, operations, or "cures" proved dangerous or worthless. It has always been willing to experiment but never when the risk to the patient seemed undesirable. But many of its experiments have been productive of new knowledge and useful techniques. It has always been willing and able to move rapidly and effectively whenever a new treatment or a new method would clearly improve patient care.

It is these same traditional and sound principles which can and should now be applied to the political, social, and economic problems of medical care. Historically, the medical profession has served under every kind of political, social, and economic system. It has considerable experience. Its goal continues to be the best medical care for the patient. It has opposed social and political experiments which it believed to be not in the best interests of the patient in the same way that it refrains from scientific experiments which carry an undue risk for a human being. It shies away from experiments which may or may not work but from which there can be no easy retreat; but it has not remained aloof from these problems; as they have become clarified and defined, the profession has carried on research. It has conducted experiments and encouraged others to do the same thing so long as the best quality in medical care for the patient was not jeopardized. There are others, mostly outside the profession, who shortsightedly have been more concerned with quantity in situations where quality should be their true goal.

There are many types of medical practice. These include traditional solo practice with the use of consultant specialists when necessary; partnerships where doctors of the same specialties are able to exchange their knowledge and experience and yet maintain a close relationship between doctor and patient; group practice where small or large groups of doctors, usually of different specialties, band together and where at times the interests of the group of doctors may tend to supersede the interests of the patient; various forms of panel practice where patients in a given medical care program must see certain doctors in order to gain the benefits of the program and where the doctor is often more responsive to the interests of the program than of the patient; insurance medicine where the doctor works for the insurance company; or government medicine where the doctor is clearly working for the government.

There are many types of medical care plans which provide varying degrees of coverage for hospital, home, office, and outpatient care; professional services; diagnostic laboratory and x-ray services; and medicaments. Other plans provide for care in clinics, clinics associated with particular hospitals, plan-operated health centers, and the like. To be satisfactory to the purchasers these plans require some degree of certainty of coverage. To be satisfactory to the administrator there must be some predictability and control of costs. To be satisfactory to the patient they should provide freedom of choice and freedom of action to both doctor and patient in the management of the patient's particular problem. In general, the more complex the program, the more the costs are increased by administrative overhead, the more the physician's effort becomes circumscribed by administrative regulation and red tape, and the more the special interest of the patient becomes subservient to the collective system.

It is not possible here to assess these medical practices and medical care plans in terms of (1) the essential elements of the best medical practice, (2) the various fallacies which seem to creep into thinking about medical care, (3) problems of abuse, administrative waste, and overhead, and (4) the ultimate costs which must be met by the individual consumer, the patient or the potential patient. It appears that to date no medical care program or system of medical practice, including traditional medicine, has been developed or proposed which entirely meets all of the desirable criteria.

In California the medical profession has taken three major experimental steps toward the solution of some of these problems. About 20 years ago it established the California Physicians' Service (Blue Shield), which was one of the earliest experiments in prepayment for hospital and physicians' services. The experience of the California Physicians' Service has been a stimulus and a guide to many other programs. In an effort to help meet the crucial problems of predictability in physician fees, the California Medical Association has carried out the Relative Value Fee Study which relates doctors' fees for various services as to one another. This study has been of fundamental importance and has made available a guide to insuring agencies for estimating doctors' usual fees for various procedures and services in various parts of the state.

San Joaquin County in California has developed what is known as the Foundation Plan for Medical Care. This has been in operation for only a little more than two years. In this program the members of the county medical association may join the foundation and agree to accept a fee based on the Relative Value Fee Study and local costs with reductions in fees for those in low income brackets. This enables the foundation in turn to contract with groups of patients for their professional care. In this program hospital care, laboratory diagnostic precedures, and medicaments are separately insured through Blue Cross, Blue Shield, or a private insurance carrier. This program interferes little with the traditional relationship between doctor and patient and with the best medical care for the patient, because the foundation includes most of the doctors practicing in the area and it provides what appears to be a workable solution for many economic and social needs.

Comment

The problems of medical practice, medical care, and modern society are in somewhat a state of turmoil. One is reminded of a boat running through a rapids. The boat is traditional medical practice. It contains the gear essential to the best care for the patient. There is no turning back. The boat must be kept upright and kept pointed toward the goal in spite of buffeting from many sides. One must keep the essential gear from falling out and too much water from splashing in. The goal, the end of the rapids, is to preserve the dignity of the patient in the personal matter of his health, to strengthen the quality of his medical care, and to adapt these fundamentals to the social, political, and economic needs of the environment.

Finally, it has been said that we are engaged in a great experiment in democracy and that it is by no means proved yet that the experiment is a success. In its concern with the welfare of its patients, traditional medicine is dedicated to making this experiment a success. It will continue to work for the best interest of the patient, who is identical in social terms with the individual human being—that often forgotten element in democracy. In this sense, the providers and the recipients of medical care are all in the same boat and are all having an exciting trip down the rapids. When the solutions to these complex problems become clear, traditional medicine will act promptly and effectively in the interest of the patient as it has always done.

909 Hyde St. (9).

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LISTERIOSIS–SUMMARY OF SEVEN CASES OF LISTERIA MENINGITIS

Herbert J. Welshimer, Ph.D.
and
Nancy G. Winglewish, B.S., Richmond, Va.

The identification of Listeria monocytogenes as a cause of bacterial meningitis often has been missed due to its morphologic similarity to nonpathogenic diphtheroids. This gram-positive-staining micro-organism was seen in the spinal fluid specimens from two of seven patients. Specific identification was made by colony study on cultures grown from spinal fluid samples of each of the seven patients. The leukocyte count in the spinal fluid was not of diagnostic value. The signs and symptoms of the three infants and four adults did not differ from those of meningitis due to other agents. This organism also causes granulomatosis of the fetus and newborn infant, conjunctivitis, urethritis, and a type of infectious mononucleosis.

Most textbooks of microbiology restrict the discussion of the bacterium Listeria monocytogenes to a few sentences or paragraphs. Such presentations lead the reader to conclude that L. monocytogenes is of little moment to the clinician. The evidence of the past few years indicates that this organism, which produces a serious meningitis in persons of all ages or fatal granulomatosis in the fetus and newborn infant, is widespread but unrecognized.

The organism was isolated by Murray and associates[1] during an epizootic in the laboratory colony of rabbits and guinea pigs at Cambridge University during the years 1923-1924. Listeria infections subsequently became established in veterinary medicine with the discovery of a variety of clinical conditions occurring in domestic animals. The infection was not recognized in humans until 1932, when the Danish investigator Nyfeldt[2] isolated the organism from patients with an infectious mononucleosis syndrome. Several years later, workers in the United States reported isolating L. monocytogenes from patients with meningitis.[3] Scattered case reports of Listeria infections in humans were published, totaling 70 cases by 1949. As a result of the studies and efforts of Dr. Heinz Seeliger, of Bonn, West Germany, and Dr. G. Potel, of Halle, East Germany, many cases of listeriosis in humans have been discovered in Germany and interest in listeriosis has mounted. Seeliger[4] lists over 200 cases of listeriosis in humans that were reported during the interval from 1950 to 1955. One index of the increased frequency of isolation of Listeria in the United States is the fact that 22 cultures were submitted to the Communicable Disease Center in Chamblee, Ga., during the five-year period from 1949 through 1954, whereas in the next three years 66 cultures were received.[5]

It is interesting that persons who have become aware of L. monocytogenes after having recognized one case of listeriosis frequently observe other cases; consequently, there are a number of reports of two or more infections observed by the same worker. Hood[6] reported 10 cases of listeriosis occurring in the New Orleans area from November, 1954, to November, 1956. By the time of publication of her article, six additional cases had been diagnosed. Dedrick[7] published a report of eight cases of Listeria meningitis that appeared in and around Los Angeles from 1952 to 1956. She since has verified an additional case. Our experience may be the reverse of other laboratories, in that we became interested in the organism before any recorded appearance of human infections in our area. Only a month after we began our studies, an organism which we identified as L. monocytogenes was isolated from a patient with meningitis. There were no further isolations of Listeria from patients until over a year later. In the next 13 months, however, L. monocytogenes was isolated from the spinal fluid of six patients; indeed, two of these patients were admitted to the same hospital within the same week.

Murray,[8] Seeliger,[4] and Hoeprich[9] have given ample descriptions listing the manifestations of listeriosis, which include meningitis, granulomatosis of the fetus and newborn infant, conjunctivitis, endocarditis, urethritis, and a type of infectious mononucleosis. Meningitis is the predominant form of listeriosis in humans both here and abroad. Fetal and neonatal granulomatosis, which accounts for a high percentage of the Listeria infections abroad, has been observed only a few times in the United States and Canada.

Summary of Cases

The table presents details of the seven cases of listeriosis that were observed in Richmond. In all of these cases small gram-positive diphtheroids were cultured from the spinal fluid and sent to us for identification. In two of these cases resident staff members performed direct examination of the spi-

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From the Department of Microbiology, Medical College of Virginia.

nal fluid by stained smears; the organisms observed were thought to be Diplococcus pneumoniae in one instance and "cocci" in the other. L. monocytogenes as seen in direct smears of spinal fluid frequently are more coccoid than bacillary in morphology and have been erroneously identified as cocci. Relative to the coccoid appearance, some workers have stated, "Very likely many cases of so-called sulfa- and penicillin-resistant pneumococcus meningitis (with the diagnosis based only on smears) are actually cases of unrecognized listeriosis. As a matter of fact, practically no case of chemotherapy resistant pneumococcus meningitis has been reported in Germany since 1951, and the number of cases due to Listeria is still increasing."[10] Easy decolorization of the organism in spinal fluid has led to presumptive diagnosis of Hemophilus influenzae[11] in gram-stained smears.

Blood cultures were negative in all but one patient (case 6; see table), a 14-day-old boy. The organism isolated from the blood was L. monocytogenes.

Summary of Data from Seven Cases of Listeriosis

Case No.	Antigenic Type Isolated	Age, Yr.	Sex	Date of Onset	Date of Admission	Symptoms on Admission	WBC in Spinal Fluid		Therapy	Outcome
							Total	% Polymorphonuclear		
1.........	1	47	M	8/6/56	8/7/56	Stiff neck, fever, disorientation	580	20	Penicillin, sulfadiazine	Discharged well 8/28/56
2.........	4	57	M	12/8/57	12/9/57	Stiff neck, fever, vomiting, irritability	1,020	58	Chloramphenicol, penicillin	Discharged well 1/15/58
3.........	4	57	M	2/17/58	2/17/58	Comatose, fever, stiff neck	980	80	Chloramphenicol, penicillin	Discharged with residual brain damage 3/14/58
4.........	4	9 days	F	4/26/58	4/27/58	Tremor, fever, irritability	...	...	Chloramphenicol, penicillin	Died 4/28/58
5.........	4	10 mo.	M	10/2/58	10/7/58	Convulsions, fever, stiff neck	1,250	63	Chloramphenicol, penicillin, sulfadiazine	Discharged well 10/31/58
6.........	4	2 wk.	M	10/6/58	10/8/58	Convulsions, fever	2,409	20	Penicillin, sulfisoxazole, chloramphenicol	Died 10/11/58
7.........	1b	64	M	12/2/58	12/4/58	Disorientation, stiff neck, fever	143	13	Penicillin, sulfadiazine	Discharged well 12/18/58

The onset, in most instances, was characterized by lethargy, anorexia, and fever followed by the rapid development of neurological symptoms for which hospitalization was sought. One patient (case 7) presented influenza-like symptoms for a period of four days. He seemed to have recovered for two days and then relapsed. Two days after the relapse he was sent to the hospital. Another patient (case 5), a 10-month-old boy, exhibited fever and anorexia for five days prior to admission. The onset of symptoms in the other patients was sudden; it preceded the hospital admission by two days in one patient and one day or less in four patients.

Some upper respiratory involvement was indicated in three of the patients: The 47-year-old man (case 1) displayed some inflammation of the pharynx. The 10-month-old boy (case 5) had a purulent nasal discharge, a slightly injected pharynx, and slightly injected nonbulging tympanic membranes. The tympanic membranes of the 9-day-old girl (case 4) were red, with questionable bulging, and the pharynx was inflamed. Upper respiratory involvement was also reported by Dedrick[7] in her observations of listeriosis. One can only speculate as to the relation of these findings to the initial focus of infection. The usual routine bacteriological procedures for handling nose and throat specimens probably would fail to draw attention to L. monocytogenes unless it was present in abundance, in which case it most likely would be dismissed as a nonpathogenic diphtheroid.

As the organisms were isolated, in vitro sensitivity tests were performed with use of commercial antibiotic disks of the following strengths: chloramphenicol, 3 mcg.; tetracycline, 30 mcg.; erythromycin, 2 mcg.; penicillin, 2 units; and dihydrostreptomycin, 10 mcg. All seven strains of Listeria were found to be sensitive to these antibiotics. Penicillin was administered in all cases together with chloramphenicol or a sulfonamide, usually sulfadiazine. The patients, with the exception of two (cases 4 and 6) who died soon after admission, became afebrile within three or four days after chemotherapy was instituted.

Serums were obtained from five of the patients at various stages of their illness and were tested for Listeria antibodies by agglutination, hemagglutination, and complement-fixation tests. No significant antibody content was detected in any of the serums. This failure to detect antibody supports Hoeprich's[9] statement, "It is a peculiarity of Listeria meningitis that recovery has not been regularly associated with demonstrable humoral antibody." Perhaps successful chemotherapy reduces the number of Listeria so rapidly as to render the antigen level unsatisfactory for significant antibody response.

The possibility of in utero transmission was considered in the cases of the two babies who died. One, a 9-day-old girl (case 4), weighing 3,430 Gm. (7 lb., 9 oz.) at birth, was delivered at full term by a midwife. The mother's prenatal course was uncomplicated. The child, one of three siblings, was progressing nicely until she began refusing formula and developed a marked tremor of the hands. On examination at hospital admission a day later, rigidity of the arms and legs was noted, with constant hyperextension of the neck and back. The temperature was 102 F (38.9 C). The child was to be given 8 million units of penicillin and 0.5 Gm. of chloramphenicol over the next 24 hours; however, she died the morning after admission. Permission for postmortem examination was not granted. Serum obtained from the mother three weeks after birth of the child was examined for Listeria antibodies by agglutination, complement-fixation, precipitin, and hemagglutination tests; antibodies were not demonstrated by any of these tests. Others have detected antibodies in mothers who have delivered infected babies. The absence of maternal antibodies, and the fact that the baby was well developed and apparently healthy, leads us to conclude that the infection was contracted after birth and not in utero. The nature of the source of infection remains undetermined.

The other baby (case 6) was a boy, 2 weeks old at the time of admission. He weighed 2,948 Gm. (6 lb., 8 oz.) at delivery by a midwife, apparently without difficulty, and use of an evaporated milk formula was started. Two days before admission to the hospital he was seen by a public health nurse when he was exhibiting seizures of a grand mal type. His mother was reported to have had epileptic seizures for many years. At the time of admission there was slight nuchal rigidity. Spinal fluid taken on admission revealed 2,400 leukocytes, with 20% polymorphonuclear cells and 80% lymphocytes. Intravenous therapy with penicillin, sulfisoxazole (Gantrisin), and chloramphenicol was attempted; seizures continued, however, and the baby died two days after admission. Permission for autopsy was not granted. Serologic examination of the mother was not performed. It is possible that this baby was infected in utero at the terminal stages of pregnancy and escaped the lethal granulomatosis reaction that is the fate of the younger and less resistant fetus.

We have examined the meconium of over 170 aborted fetuses and babies that died shortly after birth, and neither direct microscopic examination nor culture has revealed Listeria in any of our specimens.

Epidemiology

There is no indication of a common source of infection among these seven persons. Two (cases 1 and 3) lived two city blocks apart; however, they were infected with Listeria strains of different serologic types. They may have been infected from similar sources but not the same source; furthermore, there was an interval of 18 months between their illnesses.

Two patients (cases 2 and 7) lived in the same general area, but they too were infected with different serologic types and their illnesses were about a year apart. One of these men (case 2) had been deer hunting regularly up until the day before his admission to the hospital. His history revealed that he had been bitten by ticks while hunting. He and his hunting companions were impressed with the number of ticks observed both on themselves and on the deer that season. One of the hunters provided one of us (H. J. W.) with several similar ticks, which tentatively were identified as Ixodes scapularis. This is of special interest because Gray,[12] at a recent symposium on listeriosis, stated that a Russian worker reported isolating L. monocytogenes from the Old World tick Ixodes ricinus taken from cattle. Gray mentions one other report of isolation of Listeria from an insect; namely, larvae of the fly Oestrus ovis, infesting the nostrils of listeriotic sheep in New Zealand. The possibility of insect transmission of listeriosis has not received much attention; we hope to conduct studies on transmission of listeriosis by ticks.

Of the seven strains of Listeria, we tentatively have identified five strains as serologic type 4 (since confirmed by Seeliger as belonging to the subtype 4b) and one strain as type 1. The organism from one patient (case 7) is a questionable type 1 strain. The frequency of occurrence of these types is in keeping with the observations of King and Seeliger,[5] who reported that 71% of their 100 United States strains were type 4b. They isolated only one type 3 strain and no type 2 strain. Only one type 2 strain has ever been isolated and identified, that being in Scotland.

Bacteriology

L. monocytogenes is a nonsporulating, gram-positive rod, about 0.5 μ in thickness and 1 to 2 μ in length. It is aerobic, facultative, and grows over a wide range of temperatures from 4 C to 42 C, with optimal growth at 25 C to 37 C. As mentioned previously, the organism may appear coccoid in spinal fluid; however, on subculture diphtheroid morphology is assumed, with a tendency toward pallisade formation. The failure to recognize L. monocytogenes can be attributed to its morphology, which is similar to that of the nonpathogenic diphtheroids that are commonly observed in clinical specimens. The usual procedure is to regard most diphtheroids as superficial contaminants of no significance. Any diphtheroid isolated from spinal fluid should be considered L. monocytogenes until proved otherwise.

The procedure which we have used to identify Listeria is as follows: The questionable diphtheroid is transferred to brain heart infusion broth and held at 23 to 25 C; at the same time the organism is streaked on plates of tryptose blood agar base to which 1% dextrose has been added. After 18 hours' incubation the brain heart infusion broth is observed microscopically in a hanging drop preparation. L. monocytogenes is unmistakably (although not violently) motile. This feature sets it apart from most diphtheroids. At higher temperatures the organism loses its motility in a few hours. The plates are incubated at 37 C for 24 hours. They then are examined under a stereoscopic microscope illuminated with the oblique lighting technique described by Gray,[13] who observed that such illumination produces a characteristic blue fluorescence that is distinctive, although the plate may be crowded with colonies of other organisms. The blue colonies are picked and a Gram stain is prepared to check morphology. At 24 hours the colonies are 0.5 mm. or less in diameter and are transparent and convex. A characteristic buttery odor is produced by the growth on the tryptose dextrose medium. The combined findings, motility and blue colony appearance, are excellent presumptive evidence that the diphtheroid in question is L. monocytogenes.

The growth from the plate is suspended in saline solution and a spot agglutination test is performed with antiserums developed in rabbits against different antigenic types of Listeria. A more thorough antigenic study is subsequently performed by preparing H and O antigen suspensions which then are tested with specific absorbed H and O antiserums.

Carbohydrate reactions are performed in meat extract peptone broth containing 1% of the test sugar. Esculin, dextrose, salicin, and rhamnose all are fermented in 24 hours at 37 C. The fermentation of these sugars serves to differentiate L. monocytogenes from Corynebacterium species with which it may be confused.[14] Listeria strains vary in their ability to produce acid in lactose and rarely produce acid in mannitol. Four of the strains we isolated fermented lactose after 96 hours' incubation; none fermented mannitol.

Since the organisms usually are noted first on blood agar, it should be mentioned that L. monocytogenes often produces a beta type of hemolysis around the colony. This should not be used as a criterion for differentiation of Listeria from other diphtheroids, because the hemolytic activity may be extremely weak or absent.

The production of a purulent conjunctivitis, usually accompanied by keratitis, is produced in rabbits by swabbing the everted eyelid with a young broth culture of Listeria. This is highly specific and can be used for confirmation of identity; however, we feel that the procedures mentioned above are sufficient in most instances.

Comment

As indicated above, the failure to recognize L. monocytogenes probably is primarily due to its morphology, which causes it to be disregarded in the belief that it is a diphtheroid skin contaminant. In our own experience we feel that the screening of diphtheroids has been adequate; however, the probability is great that there were at least as many unrecognized cases of Listeria meningitis as there were cases in which the organism was isolated. This presumption is based on the fact that the Listeria organisms, although easily grown, in some instances may be difficult to isolate. This is exemplified in the findings of Gray and others,[15] who observed cattle suffering with brain damage that was clinically diagnosed as listeriosis. Initial cultures of the macerated brain tissue of the infected animals were negative; after the tissue was held at 4 C for a period of three weeks to three months and again cultured, however, many Listeria colonies appeared. The low-temperature incubation of spinal fluid taken from patients with meningitis of undetermined etiology might well establish some of the cases of cryptogenic meningitis as Listeria meningitis.

Summary

Seven cases of Listeria meningitis were observed in Richmond hospitals over a 2¼-year period, with six of these cases appearing in the last 13 months of the study. Two of these patients (one 9 and one 14 days old) died.

All of the patients received penicillin and at least one other chemotherapeutic agent, either chloramphenicol or a sulfonamide. All seven strains of the organism were found to be sensitive to the five antibiotics with which they were tested in vitro. Two antigenic types of Listeria were isolated.

1200 E. Broad St. (Dr. Welshimer).

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DIAGNOSTIC ERRORS DUE TO FIXED ACUTE ECG PATTERN AFTER MYOCARDIAL INFARCTION

Harris Blinder, M.D.
and
Raanan Smelin, M.D., New York

Q waves and elevated S-T segments in the precordial leads of the electrocardiogram are commonly interpreted as indicating recent myocardial infarction. In the five cases here described they were so interpreted until evidence was obtained showing that the abnormalities had existed for periods ranging from three months to perhaps eight years. The patients were four men (aged 58, 67, 67, and 69) and one woman (aged 63). Aneurysm of the left ventricle was demonstrated in two of the five patients; in one the wall of the aneurysm was calcified. The erroneous diagnosis of recent infarction resulted in prolonged, unnecessary hospitalization in all cases and to the postponement of necessary surgery on three occasions. A single electrocardiogram is not sufficient to establish the diagnosis of recent myocardial infarction because the finding of Q waves and elevated S-T segments in the precordial leads after infarction sometimes persists indefinitely.

After myocardial infarction, the electrocardiographic pattern of the acute process, with elevation of the S-T segments, may persist indefinitely in some patients. This has been termed the fixed acute ECG pattern. In these patients electrocardiograms taken months or years after the acute episode may be misinterpreted as indicating a fresh infarction. In such cases, tracings taken because of anginal syndrome or congestive heart failure as well as routine preoperative or preemployment ECG's may lead to an erroneous diagnosis of acute myocardial infarction resulting in needless or unnecessarily prolonged hospitalization.

In this paper five cases are described in which such an erroneous diagnosis was made because of the persistence of the fixed acute ECG pattern. One of these patients (case 1) was hospitalized unnecessarily after a preemployment ECG; in three cases there was needless prolongation of hospital stay (case 3, three times), and in two cases indicated surgery was unnecessarily postponed. Aneurysm of the left ventricle was demonstrated in two of the patients by roentgenogram or fluoroscopy; the patient in case 2 revealed calcification of the wall of the aneurysm 14 years after the original infarction.

Report of Cases

Case 1.—A 58-year-old man with no history of previous heart disease had an ECG (fig. 1, *top*) taken as part of a routine preemployment examination on Nov. 14, 1956. Because of the abnormal electrocardiographic findings (Q waves and elevated S-T segment in the precordial leads), the patient was hospitalized on an emergency basis, with a diagnosis of acute anterior wall myocardial infarction. Despite the absence of chest pain, abnormal physical findings, fever, or leukocytosis, the patient's condition was maintained with bed rest for four weeks. An ECG at time of discharge (fig. 1, *center*) revealed no significant change from the

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From the Cardiovascular Service, Morrisania City Hospital.

admission tracing. A follow-up ECG taken three months later (fig. 1, *bottom*) revealed persistent elevation of S-T segments. It was then apparent that the patient had not suffered an acute myocardial infarction at the time of admission but had a fixed acute ECG pattern resulting from an undiagnosed infarction in the past. It was realized that the prolonged hospitalization described above had been unnecessary.

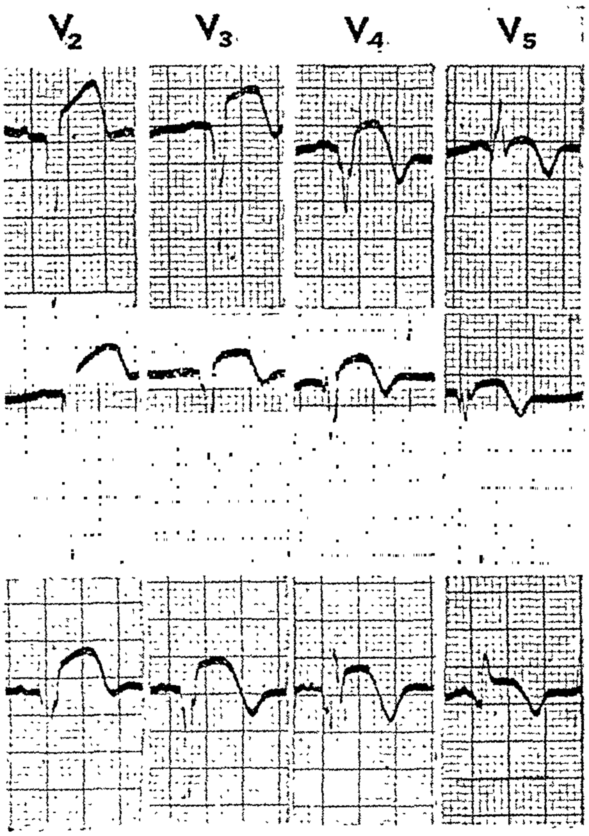

Fig. 1 (case 1).—Fixed acute ECG pattern for four-month period (*top to bottom*, Nov. 14, 1956; Jan. 2, 1957; and Feb. 7, 1957).

Case 2.—A 63-year-old woman was hospitalized on Dec. 2, 1955, because of sudden onset of dyspnea. There was a history of myocardial infarction 14 years previously. Physical examination was unremarkable except for rales and rhonchi throughout both lungs. An ECG taken on admission (fig. 2, *top*) revealed elevated S-T segments and Q waves in the precordial leads. Despite the absence of chest pain, fever, hypotension, leukocytosis, or increased sedimentation rate, a diagnosis of acute anterior wall myocardial infarction was made, primarily on the basis of the electrocardiographic findings. No serial changes were noted in tracings taken two and six weeks (fig. 2, *center*) after admission (persistence of elevated S-T segments). A roentgenogram of the chest taken six weeks after admission revealed enlargement of the left ventricle with calcification of its left lateral wall (fig. 3). It then became apparent that the patient had not suffered an acute infarction, and the final diagnosis was aneurysm of the left ventricle with calcification of its wall. It was realized that the six weeks of hospitalization had been unnecessary.

The patient was readmitted to the hospital on March 1, 1956, during an attack of acute pulmonary edema. A diagnosis of acute infarction was made on the basis of an ECG taken on admission (fig. 2, *bottom*), which revealed elevated S-T segments and Q waves in the precordial leads. However, subsequent comparison with ECG's of Dec. 2, 1955 (fig. 2, *top*) revealed a fixed acute ECG pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of fresh infarction was erroneous, and in several days the patient was discharged as improved with a diagnosis of aneurysm of the left ventricle.

Case 3.—A 67-year-old man was hospitalized on Dec. 10, 1948, complaining of severe substernal pain. Physical examination was unremarkable except for distant heart sounds. An ECG taken on admission (fig. 4, *top*) was interpreted as indicating an acute anterior wall infarction. The temperature rose on the day after admission and remained elevated for two days. The patient was kept at bed rest and was discharged after four weeks with a diagnosis of acute myocardial infarction.

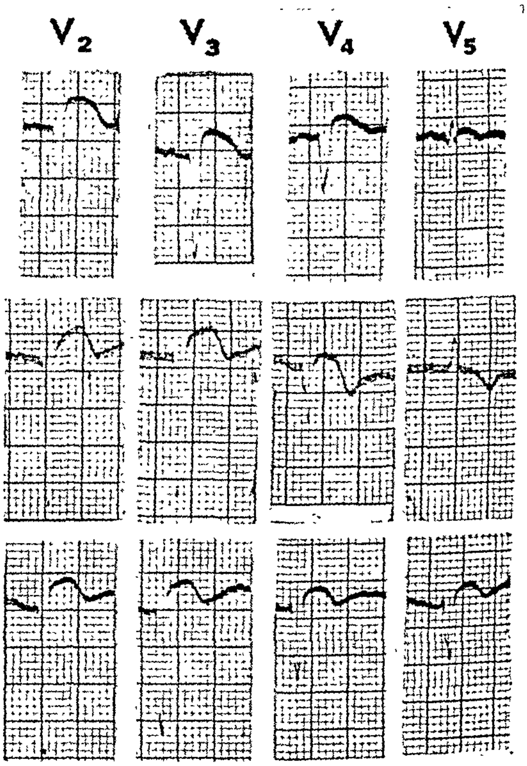

Fig. 2 (case 2).—Fixed acute ECG pattern for five-month period (*top to bottom*, Oct. 2, 1955; Nov. 16, 1955; and March 1, 1956).

The second admission was on April 10, 1953, because of urinary retention, and prostatectomy was considered necessary. An ECG on April 14 (fig. 4, *center*) was interpreted as indicating an acute myocardial infarction, and therefore the patient was kept at bed rest for one month. Surgical treatment of the prostatic hypertrophy was postponed because of the diagnosis of acute infarction.

The third admission was on Aug. 17, 1955, to the genitourinary service because of acute urinary retention. A cystotomy was performed on Aug. 18. A routine ECG taken on Aug. 22 (fig. 4, *bottom*) was interpreted as indicating acute anterior wall myocardial infarction, and because of this a second-stage prostatectomy was delayed until Oct. 14, two months after the first stage. The patient was discharged on Nov. 7.

The fourth admission was on Oct. 13, 1956, because of cough, fever, and chest pain. The initial clinical diagnosis was pneumonia. An ECG (fig. 4, *bottom*) taken on admission was interpreted as indicating an acute myocardial infarction. However, comparison with previous ECG's taken as far back as Dec. 10, 1948, revealed a fixed acute ECG pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of acute myocardial infarction made on the second, third, and fourth admissions were erroneous and that the prolonged periods of hospitalization and the delays in surgery at the second and third admissions had been unnecessary.

Fig. 3 (case 2).—Roentgenogram of left cardiac border, revealing calcification of aneurysm of left ventricle.

Case 4.—During cystoscopy for hematuria on March 20, 1957, a 69-year-old man suddenly complained of dyspnea and chest oppression, persisting for about 15 minutes. An ECG taken within one hour (fig. 5, *top*) was interpreted as indicating an acute anteroseptal myocardial infarction. Despite the observation of a fungating neoplasm of the bladder during cystoscopy, it was decided to postpone the necessary operation for six to eight weeks because of the diagnosis of acute myocardial infarction. The patient's temperature, white blood cell count, and sedimentation rate remained normal. Further questioning revealed a history of acute myocardial infarction two years previously. When the ECG's from the previous hospitalization (fig. 5, *center*) were obtained after 10 days, comparison with the current ECG's revealed a fixed acute ECG pattern (persistence of elevated S-T segments). Cystotomy was performed on April 4, 1957 (an unnecessary delay of two weeks), and a transitional cell carcinoma of the bladder was removed. A follow-up ECG taken four months later (fig. 5, *bottom*) revealed no change from the previous ECG's.

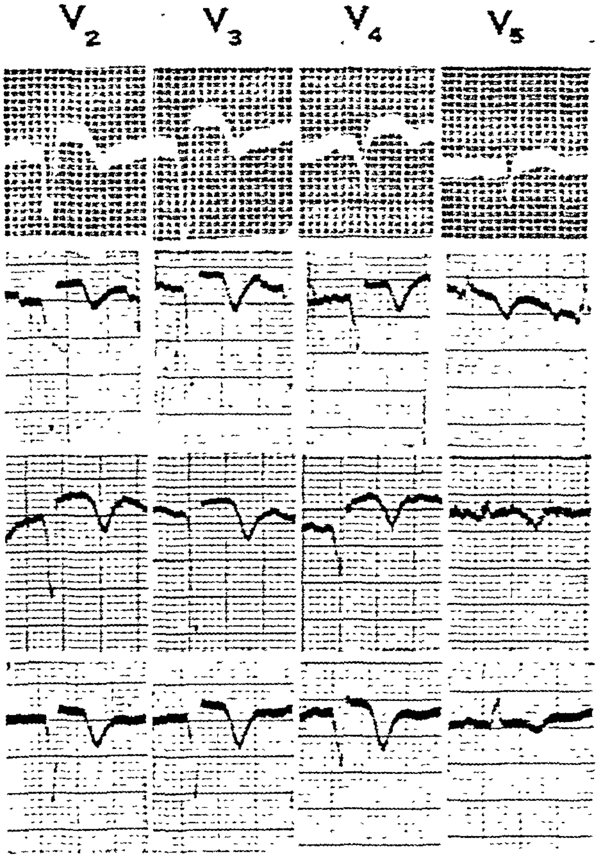

Fig. 4 (case 3).—Fixed acute ECG pattern for eight-year period (ECG's taken, *top to bottom*, Dec. 10, 1948; April 13, 1953; Aug. 22, 1955; and Oct. 13, 1956).

Case 5.—A 67-year-old man was hospitalized on Sept. 9, 1956, complaining of dyspnea and vague chest pains of six weeks' duration. There was a history of acute myocardial infarction two years previously, treated at another hospital. Physical examination revealed mild congestive failure with bibasal rales and hepatomegaly. There was a visible and palpable precordial impulse in the left fifth intercostal space, medial to the point of maximal impulse. An admission ECG (fig. 6, *top*) was interpreted as indicating an acute anterior wall myocardial infarction. There was no elevation of temperature or increase in sedimentation rate.

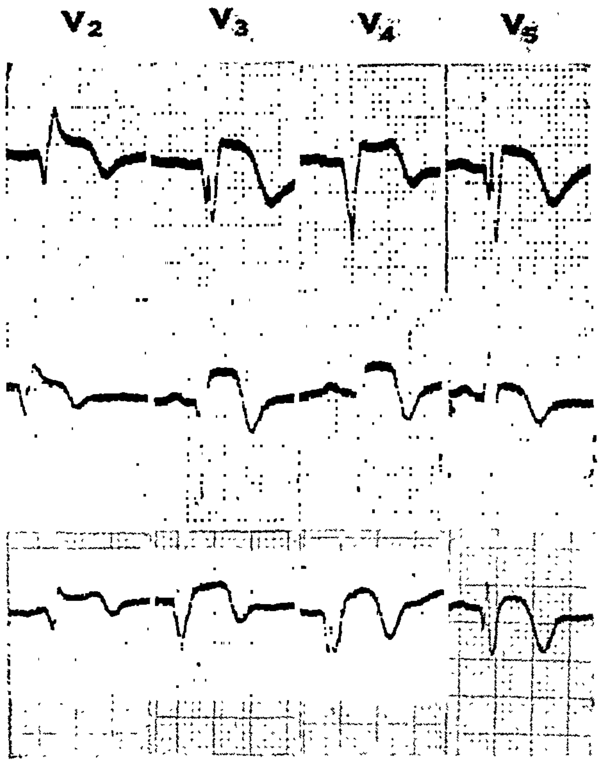

Fig. 5 (case 4).—Fixed acute ECG pattern for four-month period (*top to bottom*, March 20, 1957; June 13, 1955; and July 11, 1957).

Because of the diagnosis of acute myocardial infarction, the patient was kept at bed rest for three weeks. Fluoroscopy on Oct. 3 showed an aneurysmal bulge of the left ventricle, with paradoxical pulsation. An ECG taken on Oct. 23 (fig. 6, *center*) revealed no change from the admission ECG.

At this time the ECG's from the previous hospitalization for acute infarction in 1954 became available. Comparison of ECG's obtained during the current admission in 1956 with those of 1954 (fig. 6, *bottom*) revealed a fixed acute ECG pattern (persistence of elevated S-T segments). It was then realized that the diagnosis of acute infarction made in 1956 was erroneous and that the patient had been hospitalized unnecessarily for six weeks. The discharge diagnosis was aneurysm of the left ventricle.

Comment

After myocardial infarction in some patients, the electrocardiographic pattern of the acute process may persist indefinitely. The ECG pattern of acute myocardial infarction consists of elevated S-T segments, significant Q waves, and inverted T waves in the appropriate leads. Elevation of the S-T segments is considered to be a manifestation of acute myocardial injury and is usually presumptive diagnostic evidence of the recency of an infarction. While the Q waves and inverted T waves may remain as permanent stigmata after an infarction, the elevated S-T segments usually return to the isoelectric line within days or weeks.

In some patients the elevation of the S-T segments associated with the fresh infarction may persist indefinitely (the fixed acute ECG pattern), so that tracings taken months or years later may be misinterpreted as indicating an acute infarction,[1] resulting in diagnostic errors and unnecessarily prolonged hospitalization. The reason for the persistence of the elevation of the S-T segments in some patients is not completely understood. This fixed acute ECG pattern, however, has been noted to occur frequently in patients who develop an aneurysm of the ventricle after myocardial infarction.[2] It is probable that this relationship between ventricular aneurysm and the fixed acute ECG

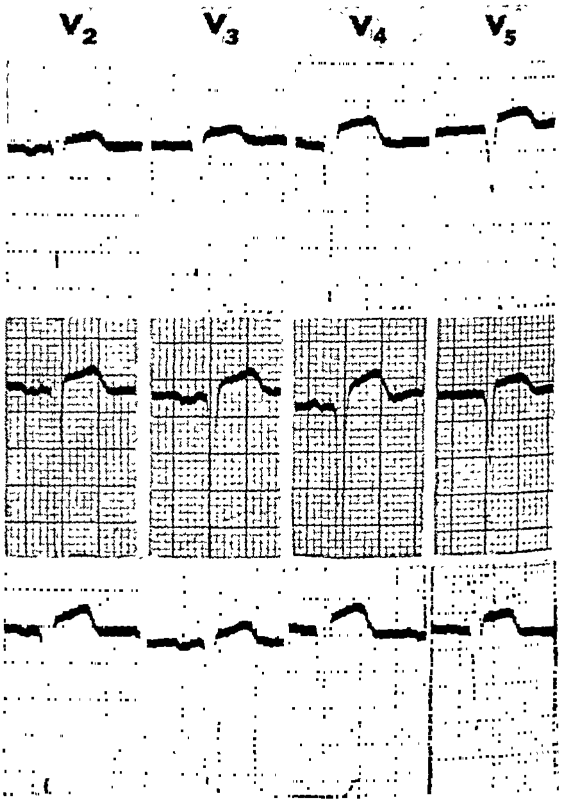

Fig. 6 (case 5).—Fixed acute ECG pattern for two-year period (*top to bottom*, Sept. 9, 1956; Oct. 23, 1956; and Aug. 7, 1954).

pattern is not coincidental, since ventricular aneurysm was demonstrated in two of the five cases presented in this paper. One must have a high index of suspicion that, in patients with an atypical history of chest pain and absence of significant clinical or laboratory evidence, electrocardiographic findings suggestive of acute myocardial infarction may represent the fixed acute ECG pattern of an old healed infarction.

Routine serum glutamic oxalacetic transaminase determinations in all cases of suspected myocardial infarction would help eliminate some of these diagnostic pitfalls.[3] The effectiveness of this procedure as a screening measure is limited by the fact that transaminase levels usually return to normal within three days after the onset of an acute infarction. Some of the diagnostic errors in the cases described above might have been avoided by obtaining some detailed histories of possible previous infarction and by the prompt comparison of admission ECG's with tracings taken at other hospitals or during earlier admissions. It should be pointed out, however, that the fixed acute ECG pattern may occur as a result of a "silent infarction" (case 1), so that even a carefully taken history may not be of value.

In patients who have recovered from acute myocardial infarction, follow-up ECG's should be taken at intervals of several months until the pattern has become stabilized. Thus, the presence of a fixed acute ECG pattern can be established and diagnostic errors may be avoided in subsequent emergency situations.

Summary

After acute myocardial infarction in some patients, elevation of the S-T segments may persist indefinitely in subsequent electrocardiograms (the fixed acute ECG pattern). In five patients this fixed acute ECG pattern resulted in erroneous diagnoses of recent infarction years after the acute event, causing needless or unnecessarily prolonged hospitalization. Aneurysm of the left ventricle was demonstrated in two of the five patients; in one the wall of the aneurysm was calcified. Care should be taken to avoid this diagnostic pitfall.

1749 Grand Concourse (Dr. Blinder).

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ACCIDENTAL RADIATION INJURY.—The characteristics of fissionable material vary with the mass and shape of the material. It is said to be "critical" when it is of such configuration that a nuclear reaction can be sustained at a fixed level of intensity. If the critical dimensions are exceeded, an exponentially increasing chain reaction will occur. Accidental excursions of this type produce variable intensities of fast neutrons and gamma rays. Accidents of this nature are referred to as criticality accidents. . . . The general consensus is that when man is exposed to a single whole-body dose of ionizing radiation, he exhibits certain clinical signs, symptoms, and laboratory findings which are collectively termed the radiation syndrome. . . . The radiation syndrome may be thought of as those clinical findings associated with total-body doses of radiation of over 100 rad. The typical . . . sequence of events following a large whole-body radiation exposure can be divided into 4 clinical stages: the initial or prodromal stage, the latent stage, the manifest illness stage, and the recovery stage. The prodromal clinical findings include anorexia, nausea, vomiting, extreme sweating, fatigue, and prostration. These changes remit in the latent period, which begins about 2 days later. After about 2 to 3 weeks of well-being a number of developments begin within a short time of one another. These may include fever, overt or occult infections, scalp hyperesthesia and epilation, purpura and hemorrhage, diarrhea, ileus, cardiovascular collapse, severe lethargy, and changes in sensorium. By about the end of the sixth week after exposure the situation has usually been resolved and clinical improvement of the surviving patients is rapid, although fatigue may continue for some time. . . . About 15% of patients exposed to a dose of 100 rad may be expected to show some of the signs and symptoms of the syndrome. The frequency increases sharply up to the level of approximately 200 rad, at which level most of those exposed would be expected to exhibit some clinical symptomatology.—G. E. Thoma Jr., M.D., and N. Wald, M.D., The Diagnosis and Management of Accidental Radiation Injury, *Journal of Occupational Medicine,* August, 1959.

PULMONARY CHANGES IN HYDANTOIN THERAPY

Matthew T. Moore, M.D., Philadelphia

The roentgenographic characteristics of diffuse fibrosis were observed as abnormal lung findings in a patient who is an epileptic. The x-ray picture remained without change for six years, and there has been no apparent correlation with pulmonary symptoms. Although the patient had no gingival hypertrophy, diagnostic study suggested that the lung tissue changes were due to a drug allergy reaction. The occasionally seen hydantoin hypertrophy of gum tissue is histologically an allergic type of change. Similar lung abnormalities were seen on 16 chest roentgenograms of 31 patients who had taken hydantoin drugs for two or more years. Six of the 15 with normal lungs had gingival hypertrophy as compared to no hypertrophy of the 16 with abnormal lungs. Selective tissue sites of allergic reaction to hydantoin drugs appear deserving of investigation.

The medical literature is replete with reports of the toxic effects of hydantoin derivatives, such as rash, gingival hypertrophy, blood dyscrasia, severe necrosis of the skin, and a wide variety of neurological symptoms which now are readily recognized as a cause-effect relationship.[1] This study deals with a more subtle type of toxic manifestation in the form of pulmonary changes appearing on the x-ray film as accentuated bronchovascular markings, or diffuse interstitial fibrosis, found in patients receiving a hydantoin preparation and which, to my knowledge, has not been reported heretofore. The substance of these observations stems from the data recorded in case 1 below, and the subsequent study of a randomly selected group of epileptic patients who have received a hydantoinate for several years.

Report of a Case

CASE 1.—This patient first came under my care on Oct. 5, 1949, at the age of 42 years. She had been treated for epilepsy since puberty with various anti-epileptic drugs and had received methoin (Mesantoin, methylphenylethylhydantoin) since 1945. The chief complaints on Oct. 5, 1949, were episodic attacks of paroxysmal abdominal pain and a diffuse, measles-like rash involving the extremities and the torso. She had discontinued medication because of the developing rash and subsequently experienced the seizures of abdominal pain. The rash was considered to be due to the methoin, and withdrawal of the drug resulted in complete elimination of the skin eruption, but this was followed by the bouts of abdominal epilepsy.[2] Diphenylhydantoin (Dilantin) sodium was substituted for the methoin, and the attacks of paroxysmal abdominal pain ceased. In a relatively short time she developed an intolerance to diphenylhydantoin in the form of severe ataxia, visual disorder, and speech defect, necessitating a return to therapy with methoin in smaller dosage in combination with a barbiturate, on which she has remained, seizure-free. On April 21, 1953, the patient sustained minor injuries in a taxicab accident, and on May 4, 1953, complained of pain in the left side of the chest, posteriorly. Although no evidence of pulmonary disorder was apparent on physical examination, an x-ray of the chest was obtained. This was reported by Dr. Jacob H. Vastine II, as follows: "There is mottling throughout all of the lung fields suggesting a tracheobronchitis, pneumonitis or possibly an allergy. This is not the usual appearance of tuberculosis, although this patient should be kept under observation and reexamined in 4 weeks." The chest pain disappeared shortly thereafter and, the patient being symptom-free, x-ray studies were not repeated. During the early part of 1954 symptoms of pelvic disorder developed, and on July 26, 1954, a hysterectomy was performed for removal of a large uterine fibroid. The viscera were adherent to the uterine mass, requiring meticulous stripping of the gut from the uterus and adnexa. Convalescence was relatively slow. Pain in the left side of the chest made its appearance again on Sept. 24, 1954, and once more roentgenographic study of the chest was done by Dr. Vastine. The report, in part, read: "Films of the chest show mottled infiltration throughout all of the lung fields. This has not changed appreciably during the past 16 months (fig. 1). The nature of this is not evident. It is probably due to an allergy (Loeffler's pneumonitis). There is nothing which can be interpreted as tuberculosis, neoplasm nor other pulmonary pathology."

It was at this point that the significance of the interpretation of the roentgenographic findings, as possibly due to an allergic phenomenon, occurred to me. I knew of the references in the literature regarding the etiology, pathogenesis, and pathology

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From the Graduate School of Medicine, University of Pennsylvania.

of gingival hyperplasia incident to hydantoin therapy, and that several authors considered the epithelial and collagen hypertrophy to be of allergic origin.[3] Moreover, the patient had normal gums. Why then could not the roentgenographic findings represent proliferation of the epithelial and collagen components of the bronchioles and/or vascular collagen disease similar in nature to that evident in the gums of some patients receiving hydantoin preparations? To test the validity of this concept, 30 additional patients who were on diphenylhydantoin and/or methoin therapy were studied.

A dramatic epilogue to the history of the patient during December, 1958, and January, 1959, highlights the necessity of recognizing the role of hydantoin in producing a form of pulmonary fibrosis, because of the alarm and expense to the patient and the apparently unnecessary array of studies and consultations which were done in hospital. During the latter part of December, 1958, while vacationing in Florida, the patient developed an upper respiratory infection with cough and respiratory distress. The symptoms cleared after two weeks while she was taking an antibiotic. On Jan. 26, 1959, she experienced a mild chill, associated with a cough, and an x-ray of the chest was made at a Miami hospital. She was informed of the scattered opacities in the chest and told they were quite serious. The physician suggested that she return to Philadelphia at once for further study and treatment. She consulted an internist, who admitted her to the Graduate Hospital, University of Pennsylvania, on Jan. 29, 1959. Here extensive hematological studies, heterophil antibody studies, agglutination tests, bacteriological investigations, and roentgenographic studies of the chest and kidneys were carried out. Numerous consultants examined her. During her stay in hospital she was free from pulmonary symptoms. The only finding of significance in the many studies was the scattered mottling of pulmonary fibrosis which corresponded with the films of May 4, 1953, and Sept. 24, 1954. The report of the x-ray department concluded: "In view of the clinical history and previous studies made elsewhere, this may represent some unusual allergic reaction. However, the findings themselves are consistent with sarcoidosis, Loeffler's syndrome, eosinophilic granuloma, or even a granulomatous process such as tuberculosis or fungus. The chest is otherwise negative" (fig. 2). The internist summarized his findings on Jan. 3, 1959, by saying: "There is a remarkable disproportion between symptoms and signs and the extensive pulmonary changes. Tuberculosis, fungal infection, sarcoidosis, lupus erythematosus must all be excluded." After studies were completed he made the final comment: "Without biopsy, I should suggest a diagnosis of suspected

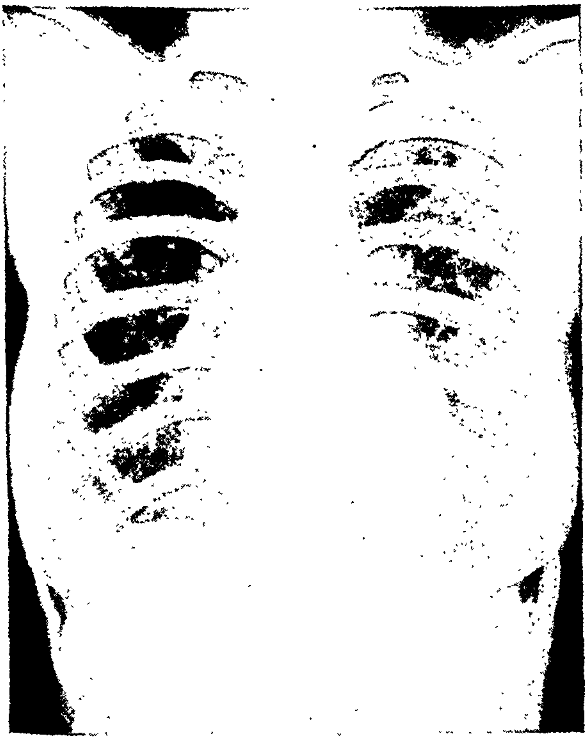

Fig. 1 (case 1).—Sept. 24, 1954. Mottled areas diffusely scattered throughout both lung fields. Identical to film taken May 4, 1953.

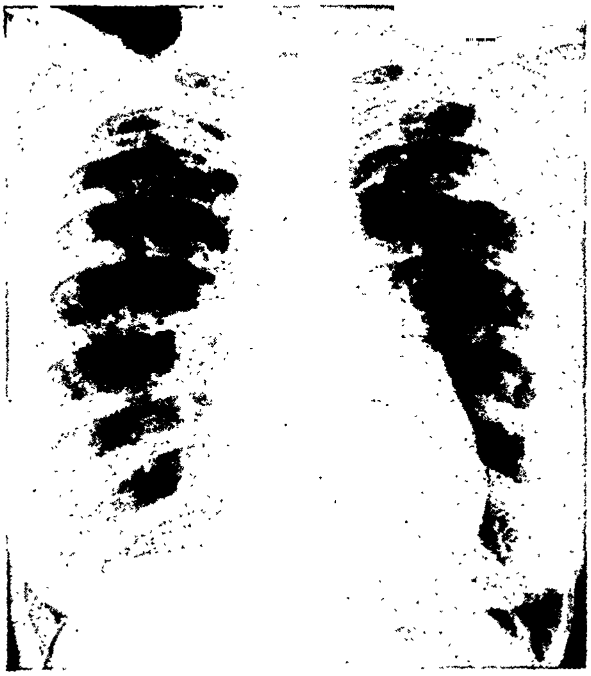

Fig. 2 (case 1).—Jan. 26, 1959. Pulmonary changes are similar to those in figure 1. Gums normal.

pulmonary fibrosis, cause undetermined. Consider patient non-infectious." She was discharged from hospital asymptomatic, and has remained so to date.

Material and Method

Thirty-one patients were selected at random from a larger series of private patients who were receiving a hydantoin preparation, either singly or in combination with a barbiturate, trimethadione (Tridione), primidone (Mysoline), or occasionally amphetamine sulfate. The roentgenographic studies of the chest were done with use of the usual technique. Roentgenographic studies of three patients were done in hospitals, and studies of the remaining 28 were done in a private x-ray laboratory. There were 18 males and 13 females, ranging in age from 13 to 59 years. Twenty-eight of them received diphenylhydantoin sodium, 24 getting diphenylhydantoin only, and 4 a combination of diphenylhydantoin and methoin; 7 patients used methoin, of whom 3 had methoin alone. These patients had received some form of hydantoin continuously prior to this study for periods of from 2 to 12 years. In 27 of these patients there had been no other occasion to perform roentgenographic studies of the chest than for the purpose of this study. The other four cases consisted of case 1, in which the pulmonary fibrosis was a fortuitous finding and diagnosed as stated above; case 22, in which the patient was undergoing extensive study in hospital to determine the cause of convulsive seizures (which proved to be a hemorrhagic cyst of the brain) and in which the chest films were negative; case 26, in which findings on chest films, made in a general hospital, were interpreted as "pulmonary fibrosis"; case 30, in which the patient was an epileptic who had a psychotic episode, and in which chest films made while he was in a psychiatric hospital were interpreted by the roentgenologist on two occasions 19 days apart as "severe accentuation of bronchovascular markings extending into all lung fields—acute tracheobronchitis" (fig. 3). All of the chest films were interpreted by the same roentgenologist on a scale which we rated as follows: 0 = none, + = mild, ++ = moderate, and +++ = severe accentuation of the bronchovascular markings or pulmonary interstitial fibrosis. Similar ratings for the gingival changes were made separately, and the results of both evaluations were tabulated.

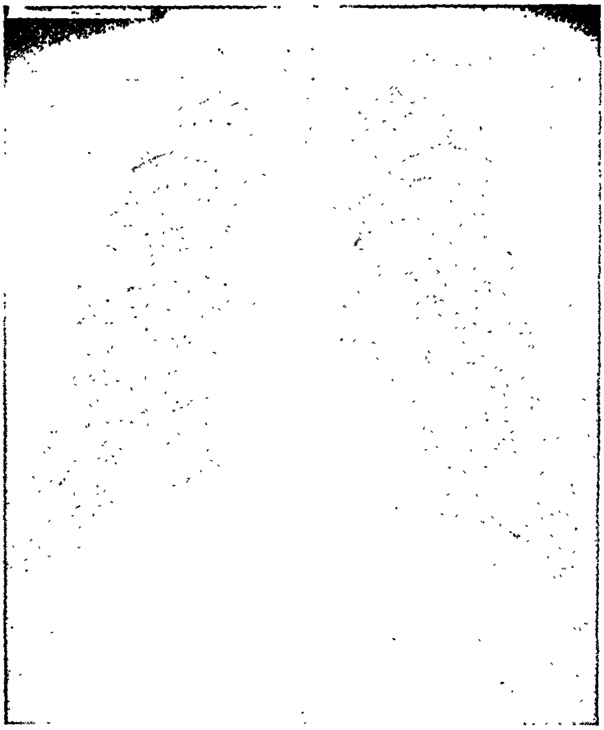

Fig. 3 (case 30).—"Severe accentuation of bronchovascular markings extending into all lung fields." Interpreted as "acute tracheobronchitis." Gums normal.

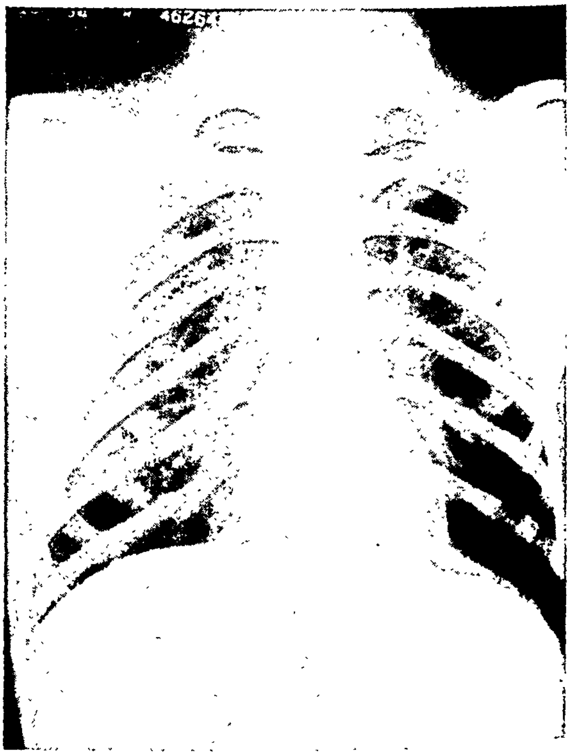

Fig. 4 (case 25).—Oct. 1954. Marked accentuation of bronchovascular markings in all lung fields. Repeat film December, 1955, unchanged. Gums normal.

Pulmonary changes were present, in degrees varying from mild (11 patients) to moderate to severe (16 patients), in a total of 27 patients, or 87%, and gingival hyperplasia was absent (17 patients) or mild (8 patients) in 25 patients, or 80.6%. In the table it will be seen that in those patients presenting moderate to severe lung changes (16 cases) gingival hyperplasia was not present at all in 13 and was only mild in 3 instances (fig. 4). Of six patients who exhibited moderate to severe gingival hyperplasia five showed mild lung changes and one showed none (fig. 5, 6, 7, and 8). In only one patient (case 29) was there a combined absence of lung and gingival involvement. Two patients with mild gingival overgrowth showed no lung changes; three patients without gingival changes showed mild pulmonary fibrosis; and three with mild gingival hyperplasia showed a mild counterpart in the lung.

Scale of, and Relation Between, Pulmonary and Gingival Changes in Thirty-one Patients on Hydantoin Therapy

			Scale of Changes*	
Case No.	Sex	Age, Yr.	Gingival (Hyperplasia)	Pulmonary† (Accented Bronchovascular Markings or Diffuse Pulmonary Fibrosis)
1	F	50	0	+++
2	F	39	+	0
3	F	38	+	++
4	M	41	0	++
5	M	58	0	++
6	M	35	+++	+
7	F	42	0	++
8	F	59	+	+
9	M	46	0	+++
10	F	48	0	+
11	M	13	++	+
12	M	50	++	+
13	M	33	0	++
14	M	18	+	+
15	M	33	0	++
16	F	18	+++	+
17	M	33	0	+++
18	M	35	0	++
19	M	15	+	++
20	F	19	+++	+
21	M	18	+	+
22	F	25	+	0
23	M	38	0	+
24	M	57	0	++
25	M	22	0	+++
26	F	47	+	+++
27	M	31	0	+
28	F	43	0	++
29	F	28	0	0
30	M	36	0	+++
31	F	16	+++	0

* Scale: 0=none; +=mild; ++=moderate; +++=severe.
† Shown roentgenologically.

From the above it would appear that there is an inverse relation between the occurrence of pulmonary fibrosis and gingival hyperplasia. By inference, when the target organ is the lung, the gums escape, and if the latter are involved there is minimal or no pulmonary involvement. Thirteen per cent of the patients had normal lung fields as shown by roentgenographic examination.

Comment

The observation, as seen in the table, of the presence of pulmonary changes in those patients in whom the gum structure is normal, and the reverse in those having gingival overgrowth, can be attributed to more than mere statistical chance. The structural tissue components common to both gums and bronchioles are epithelial cells, collagen fibers, and small blood vessels. Histological examination of both human and experimental animal hydantoin-hypertrophied gum tissue reveals the overgrowth to be due mainly to marked epithelial proliferation and extreme hyperplasia of collagen fibers (fig. 7 and 8). In addition, there is an increase in the size and number of blood vessels

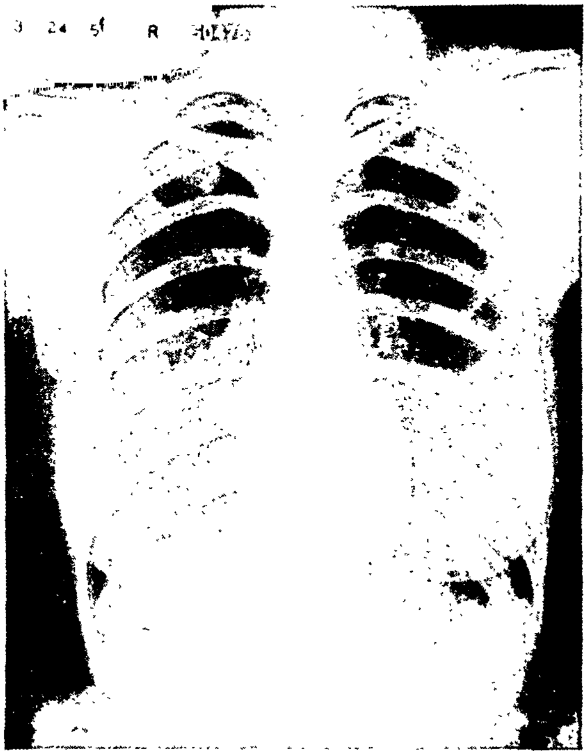

Fig. 5 (case 20).—Minimal prominence of bronchovascular markings in lower lung fields—not in upper. Intense gingival hyperplasia (see figure 6).

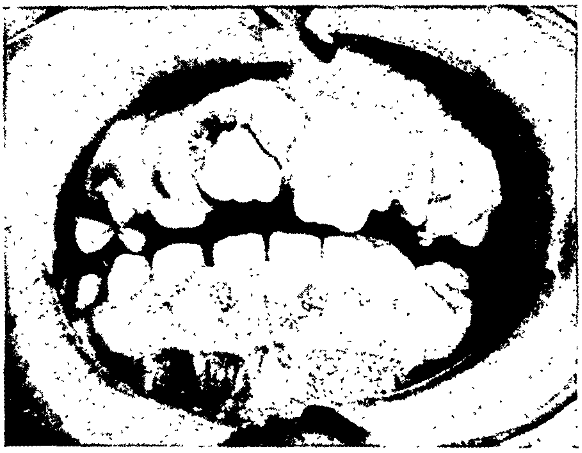

Fig. 6 (case 20).—Advanced gingival hydantoin effect.

and lymph channels, as well as varying degrees of inflammatory reaction in the corium.[4] King noted these changes in ferrets given diphenylhydantoin and also called attention to the significant finding of vasodilatation and perivascular proliferation of fibroblasts.[4b] Numerous references have been made indicating that the gingival hyperplasia in patients receiving a hydantoinate is the result of a sensitization process.[3] Since the bronchiolar system has tissue elements similar to those of the gums, it is surmised from the data offered here that the target organ of the sensitization process, in the main, is the lung when the gums are not affected.

When interpreting a chest film, the roentgenologist, lacking the history of a patient, not infrequently renders the nonspecific diagnosis of "bronchovascular markings accentuated beyond normal," or "diffuse interstitial pulmonary fibrosis." These pulmonary findings can be observed as the result of a large variety of causes, among which are some of the so-called man-made diseases [5] secondary to the administration of hexamethonium chloride or hydralazine compounds,[6] drug sensitization resulting in polyarteritis nodosa,[6] and the type of pulmonary changes reported here following hydantoin medication. An inventory of other conditions which may produce the roentgenologic appearance of "pulmonary fibrosis," or diffuse mottled areas of increased "bronchovascular markings" would include histiocytic reticuloendotheliosis [7]; pulmonary hemosiderosis [7]; polycythemia [7]; miliary sarcoidosis [7]; histoplasmosis [8]; coccidiosis; sinobronchitis; tracheobronchitis; allergic diseases [7] such as bronchial asthma, hay fever, angioneurotic edema, eczematoid dermatitis; Loeffler's syndrome [9]; collagen diseases such as polyarteritis nodosa, disseminated lupus erythematosus, scleroderma, dermatomyositis; such other skin disorders as erythema multiforme, erythema nodosum [7]; diffuse interstitial fibrosis of the lungs (Hamman-Rich syndrome) [10]; and nickel carbonyl [11] and beryllium poisoning.[12]

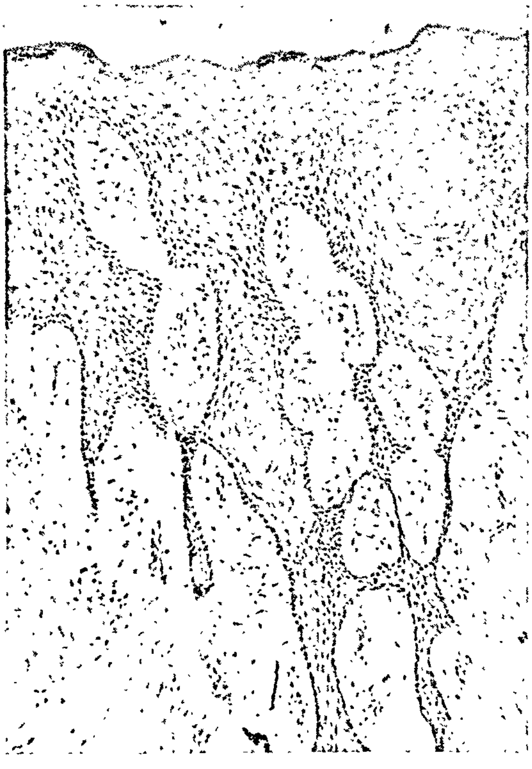

Fig. 7 (case 31).—Advanced gingival overgrowth. Pronounced epithelial hyperplasia with rete-peg and whorl formation extending well into corium. No pulmonary changes. (Hematoxylin and eosin stain × 100.)

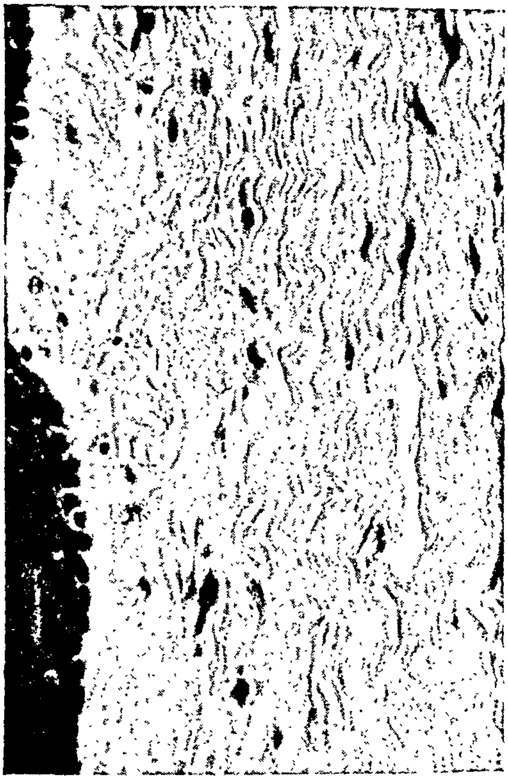

Fig. 8 (case 31).—Extreme hyperplasia of collagen fibers in corium of gum. (Mallory tri-chrome stain × 400).

Unless the internist and roentgenologist are aware of the relation between the lung findings and the hydantoin effect, they could very well submit diagnoses which would include some of the above and hence be far afield, with the resulting visitation on the patient of dismay, uncalled-for expense, and perhaps erroneous or unnecessary treatment.

Summary and Conclusions

Of a group of 31 epileptic patients on hydantoin therapy, 87% showed pulmonary changes roentgenologically in the form of "accentuated bronchovascular markings" or "diffuse pulmonary fibrosis." There appears to be an inverse relation between these findings and hydantoin gingival hyperplasia. The possible pathogenesis of this form of pulmonary disturbance must be recognized to avoid erroneous diagnosis and treatment.

1813 Delancey Pl.

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Grateful acknowledgment is made to Dr. Jacob H. Vastine II for the roentgenologic interpretations and ratings.

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ACQUIRED HEMOPHILIA B

REPORT OF CASE WITH DIAGNOSTIC LABORATORY FINDINGS

Seymour Gollub, M.D., Houck Bolton, M.D., Edmund Hessert, M.D.
and
Alexander Ulin, M.D., Philadelphia

A 22-year-old man was hospitalized with complaints of dyspnea and hemoptysis and a history of heart disease and coagulation defects. Repeated study of the clotting mechanism showed the outstanding deficits to be those of thromboplastin generation characteristic of hemophilia B. When the patient's cardiac failure and hepatic dysfunction were relieved, the coagulation defect also disappeared. The hemophilia in this case, therefore, was not hereditary but acquired.

The clinical criteria for the establishment of the diagnosis of classic hemophilia include a bleeding tendency dating from infancy, male sex, a family history of similarly affected males, and transmission of the defect by an apparently normal female. Until recently, laboratory findings of a normal one-stage prothrombin time, prolonged whole-blood clotting time, and a normal platelet count completed a "rigorous diagnosis" of hemophilia. However, with advances in knowledge and the establishment of more precise diagnostic laboratory tests, our understanding of the syndrome has advanced beyond this

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From the Blood Coagulation Research Laboratory, Hahnemann Hospital and Medical College, Philadelphia, and West Jersey Hospital, Camden, N. J.

simple formulation. The fact that in approximately one-third of the cases no family history of the expected inheritance pattern was obtainable, and the occurrence of bona fide female hemophiliacs,[1] could not be reconciled with the original formulation.

The demonstration by Pavlowsky[2] in 1947 that plasma samples from different patients with hemophilia could mutually correct each other brought further depth to the problem of hemophilia and suggested the existence of different pathological conditions grouped under the clinical syndrome designated by the single term hemophilia. This situation was greatly clarified by the introduction of the thromboplastin generation test of Biggs and Douglas.[3] As a result of this work it was shown that two distinct pathological entities with similar inheritance patterns, each due to the lack of a different specific protein function occurring early in the coagulation process, gave rise to two indistinguishable clinical conditions. The new pathological entity has been well established and is known as hemophilia B,[4] or Christmas disease. At least four related hemophiloid conditions have been reported.[5] The necessity of the hereditary pattern in the diagnosis of hemophilia is undetermined at present. It has been said that true hemophilia occurs sporadically in 25 to 30% of the total cases recorded. This condition is probably due to mutation, so that hemophiliac males or females arise *de novo*.[6]

Stefanini and Dameshek[7] reported studies in a young woman in whom it was possible to demonstrate deficiencies of both prothrombin and antihemophilic globulin but who had no demonstrable hereditary hemostatic defect. He cited other such cases of apparently acquired hemophilia, one showing spontaneous recovery some months after hemorrhagic symptoms and definitive laboratory studies.

It is the purpose of this paper to report a case of apparently acquired hemophilia B associated with long-standing cardiac failure in a young man undergoing evaluation for corrective surgery. With relief of cardiac failure there was apparent spontaneous recovery, evidenced by lack of hemorrhage or unusual bleeding manifestations at definitive cardiac surgery.

Our materials and methods have been detailed elsewhere.[8] In general, laboratory methods of coagulation analysis have been used in accordance with generally accepted descriptions.[9]

Report of a Case

A 22-year-old man was admitted to the thoracic surgical service of the West Jersey Hospital with a history of long-standing rheumatic valvular heart disease, intermittent cardiac failure, and coagulation deficiencies. Medical history revealed no evidence of cardiovascular disease until the age of 12 years, when he was told he had a murmur and an enlarged heart after an episode of pneumonia.

In May, 1955, he was hospitalized because of progressive exertional dyspnea and repeated bouts of hemoptysis. Physical examination at that time revealed a blood pressure of 130/80 mm. Hg and normal pulmonary findings. The apical cardiac thrust was located outside the midclavicular line in the fifth left intercostal space. Aortic systolic and mitral diastolic thrills were readily palpable. Auscultation revealed a diminished aortic second sound and an accentuated mitral first sound, and at the apex a loud mitral opening snap with a rumbling mitral diastolic murmur and a soft mitral systolic murmur. The liver was unremarkable and the spleen was slightly enlarged and nontender. Fluoroscopic examination of the heart demonstrated a straight left border with an enlarged left atrium in conjunction with lung fields suggesting chronic passive congestion and hemosiderosis. The electrocardiogram showed a wandering pacemaker with a rate varying between 50 and 60 beats per minute. At this time cardiac catheterization was deferred on the basis of an abnormal coagulation evaluation which revealed platelets in the range of 80,000 per cubic millimeter, with decreased prothrombin consumption, abnormal clot retraction, and altered thrombin generation. The serum electrolyte and bilirubin levels were within normal limits, as was the result of the pulmonary function study. The patient was instructed to return to hematology clinic for continued study.

In the ensuing two years, while he was employed as an engineer, the patient's condition gradually deteriorated. He experienced several bouts of questionable heart failure for which he was intermittently digitalized. His exertional dypsnea increased, and the frequency and severity of his bouts of hemoptysis became marked. His hematological picture remained essentially unchanged. In Febuary, 1957, and in November, 1957, the patient underwent repeated cardiovascular surveys at our hospital at which times the physical findings, as noted on his previous admission, were present and in most cases aggravated. During this period the patient underwent repeated study by our coagulation research laboratory for definitive diagnosis of his coagulation defect. In March, 1958, the patient was readmitted with severe palpitations, marked shortness of breath, abdominal pain associated with coughing, and frothy hemoptysis. Physical examination at the time revealed an acutely ill young man in obvious congestive heart failure. The cardiac rhythm was absolutely irregular at a rate of 130 beats per minute. There was a grade-2 systolic murmur heard in the aortic area and an aortic diastolic murmur. The liver was palpated 4 fingerbreadths below the right costal margin. It was hard and nontender. There was a 2+ pitting ankle edema. An electrocardiogram revealed atrial fibrillation and flutter with a ventricular rate of 130 per minute. Roentgenologic examination demonstrated 3+ general cardiac enlargement, with widespread congestive changes throughout both lung fields. Hospital laboratory studies obtained at that time revealed thymol turbidity, 4 units, and cephalin flocculation, 2+. The patient responded well to treatment and on discharge in May, 1958, he was out of heart failure, effectively digitalized, and free of acute symptoms. The liver and spleen were not palpable. There was no dependent edema and the lungs were essentially clear. The abdomen was normal, and the patient gained weight.

At the end of May, 1958, the patient successfully underwent intracardiac catheterization and several days later tolerated thoracic aortography without evidence of bleeding. The clinical diagnosis of major mitral and aortic stenosis and minor aortic insufficiency was substantiated. In June, 1958, the patient underwent definitive surgery, consisting of transventricular aortic valve dilation and mitral commissurotomy through the left atrial appendage. Hemostasis was secured by electrocoagulation. The patient withstood the operative procedure well and was returned to the recovery room in good condition. Blood loss during the operation was minimal and there was no evidence of abnormal coagulation encountered during or after the operative procedure. His postoperative course was uneventful and uncomplicated. Up to the time of writing the patient has been well and asymptomatic.

Table 1.—*Results of Coagulation Studies Made Between February, 1957, and January, 1958*

	2/27/57		3/6/57		1/10/58*	
	Control	Patient	Control	Patient	Control	Patient
Platelet count, per cu. mm.		190,000		194,000		160,000
One-stage prothrombin time, %	100	62	100	85	100	65
Recalcified clotting time	4'20"	7'53"	2'	2'23"	2'15"	3'23"
Inhibitors	5'22"	4'46"(neg.)	2'30"	2'56"(neg.)	2'25"	2'42"(neg.)
Prothrombin consumption, %	83	80	...	...	83	70
Factor VII, %	130 enh.†	140 enh	...	...	130 enh.	0 enh.
Factor V, %	100	91	...	...	100	100
Fibrinogen, mg. %	165	153	284	268		168
Thromboplastin generation, %	100	22	100	32	100	53

* A lysin determination carried out at this time was negative at 24 hr. for both control and patient.
† Enh: enhancement.

Results.—In table 1 may be seen the results of the coagulation studies done over a period of approximately 10 months, February, 1957, to January, 1958, during which the patient was treated repeatedly for heart failure. The initial study in February, 1957, shows the following outstanding features: mild hypoprothrombinemia, moderately severe thromboplastin generation depression, and prolongation of the recalcified plasma clotting time. Results of further laboratory studies done to find precisely the nature of the coagulation defect are shown in table 2, where it may be seen that the defect in thromboplastin generation resides in the patient's serum and is corrected by normal serum but not by serum from a patient with hemophilia B. Also shown in table 2 are the plasma recalcified clotting times when various normal and deficient plasmas were mixed in proportions of 1:1. These indicate that the patient's plasma does not inhibit the coagulation in normal plasma; that the patient's plasma and the plasma of a patient with hemophilia A are mutually corrective; and that the patient's plasma and the plasma of a patient with hemophilia B are not mutually corrective. Further studies on the patient shown in table 1 done in March, 1957, and January, 1958, show some variation in several of the tests. The most outstanding deficits, however, are those of thromboplastin generation in March, 1957, and thromboplastin generation and factor VII in January, 1958. Special studies done in March, 1957, and January, 1958, on the specific deficit in thromboplastin generation were in general consistent with the studies already referred to.

Table 2.—*Results of Further Studies to Determine Nature of Coagulation Defect, Made in February, 1957*

	Control	Patient
Thromboplastin generation corrections, %		
Patient, alone	...	22
Hemophilia B sample, alone	10	...
Normal alumina plasma and test serum	100	25-28
Normal serum and test alumina plasma	100	62-58
Test serum, 1:1 with normal serum and normal alumina plasma	100	84
Test serum, 1:1 with hemophilia B serum and normal alumina plasma	...	23
Plasma recalcified clotting times*		
AHG deficient	10'	...
PTC deficient	5'14"	...
Patient	5'4"	...
Patient and AHG deficient	...	3'25"
Patient and PTC deficient	...	4'35"

* AHG = antihemophilic globulin; PTC = plasma thromboplastin component.

Table 3 shows the detailed results of coagulation studies made during a cardiac operative procedure after the patient had been successfully treated for heart failure. It will be noted that four samples were taken: an initial sample before surgery, a sample during surgery, a two-hour postoperative sample, and a 24-hour postoperative sample. Also included are analyses of the three bottles of blood the patient received over a 24-hour period. It will be noted that the results of these studies are essentially normal. Thromboplastin generation values in particular are within normal limits of our laboratory. The prothrombin consumption values of the initial sample may perhaps be said to be the only abnormal finding. However, we have not found this test to correlate well with the thromboplastin generation test in our hands.

Comment

Data have been presented indicating the existence of a coagulation defect, identical in results of laboratory tests to the defect known as hemophilia B, in a young man who had no family or personal history of a bleeding tendency. The severity of the defect was somewhat variable over the course of 10 months, but it was definitely present. The alleviation of the state of chronic cardiac failure prior to definitive surgery seems correlated with the disappearance of the coagulation abnormality. Lack of unusual bleeding tendency during and after thoracotomy further emphasized the patient's intact hemostatic mechanism at the time of surgery. The period of time prior to surgery in which laboratory studies were done extended back almost 15 months. From the laboratory point of view there can be little doubt that this patient's defect was identical to that seen in hemophilia B. Indeed, studies done in another institution on this patient were compatible with a diagnosis of hemophilia as long as two years prior to cardiac surgery. It is not our intention to enter into a discussion of the propriety of the particular type of nomenclature to be used in this case. However, it seems clear that the patient in this study shows clinical and laboratory evidence of an impairment in thromboplastin development, due to a functional deficiency of the factor lacking in the condition known as hemophilia B. Further, clinical and laboratory evidence suggest the disappearance of this defect to be associated, in time at least, with the alleviation of the state of chronic cardiac failure and hepatic dysfunction. It is tempting to speculate that the coagulation defect was related to hepatic dysfunction due to chronic cardiac failure.

TABLE 3.—*Results of Subsequent Coagulation Studies**

	Control	Before Surgery	During Surgery	2 Hr. Postoperative	24 Hr. Postoperative	1st Citrate Bottle	2nd Citrate Bottle	3rd Citrate Bottle
Platelets		160,000	148,000	190,000	190,000	180,000	310,000	140,000
One-stage prothrombin time, %	100	68	90	100	100	85	100	83
Recalcified clotting time	3'27"	3'10"	1'41"	1'57"	2'55"	3'12"	2'2"	2'27"
Inhibitors	2'45"	2'42"	1'52"	1'45"	2'5"	2'37"	1'50"	1'57"
Prothrombin consumption, %	100	66	...	...	...	...	...	...
Factor VII, %	100	56 enh.†	...	240 enh.	105 enh.	...	...	...
Factor V, %	100	...	...	...	...	...	...	...
Fibrinogen, mg. %	320	188	200	215	275	165	220	145
Thromboplastin generation, %	100	87	95	96	86	89	84	72

* Lysin determinations (24-hr.) were negative throughout.
† Enh: enhancement.

Summary

An acquired state of impaired coagulation, with diagnostic laboratory findings identical with those of hemophilia B, occurred in a patient without family or personal history of hemorrhagic or bleeding tendency. Concomitant with the alleviation of chronic cardiac failure and hepatic dysfunction the patient's coagulation studies showed a return to normal, and lack of clinical evidence of impaired coagulation was shown by minimal bleeding encountered during and after definitive thoracic surgery.

230 N. Broad St. (Dr. Gollub).

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CLINICAL NOTES

ASYMPTOMATIC TUBERCULOUS ENTERITIS SIMULATING CARCINOMA OF THE CECUM

Hubert U. Waggener, M.D., James P. Muldoon, M.D.
and
J. Richard Heaton, M.D., Grand Rapids, Mich.

The ileocecal region is the most common site affected in patients with tuberculous enteritis. The roentgenographic studies may show resemblances to carcinoma. The disease is generally seen in patients with advanced cases of pulmonary tuberculosis, and symptoms are ordinarily present. Tuberculosis limited to the intestine is usually of the bovine type. It is rare to see a patient with active pulmonary tuberculosis and extensive tuberculosis of the ileocecal region without symptoms and suggestive physical findings. The following case report is of tuberculous enteritis in a healthy-appearing adult male with a minimal anorectal complaint.

Report of a Case

A 38-year-old man entered the hospital on April 1, 1959, with a chief complaint of an annoying discharge from "near the rectum" of three months' duration. There were no other complaints. Elaboration of the present illness and an extensive review of the systems yielded no additional symptoms. He had been working 8 to 10 hours per day for the past six years. A "spot on the right lung" had been present for 12 years. Periodic chest roentgenograms had showed no change through 1957, according to the patient. He denied any family history of tuberculosis. On physical examination the patient appeared to be a well-developed and well-nourished man in no distress. The only abnormal finding was confined to the anus. Adjacent to the left posterior quadrant was a 2.5-cm. linear ulceration with overhanging edges. Anoscopic and sigmoidoscopic examinations showed negative results.

Results of all blood and urine studies were normal. Roentgenographic examinations of the colon with use of barium enema revealed a persistent, large filling defect of the middle of the ascending colon, strongly suggesting a primary colonic neoplasm (fig. 1). A roentgenogram of the chest (fig. 2) was originally interpreted by the radiologist as showing fibrocalcific deposits in the upper lung fields secondary to a previous tuberculous process but without evidence of activity.

An operation was performed on April 6, 1959, with a preoperative diagnosis of adenocarcinoma of the ascending colon. A large, firm, irregular, and constricting lesion of the ileocecal region was found. Multiple loops of distal ileum adhered to this area and were segmentally involved by direct extension of the lesion. Small, narrow, and nodular lesions encircled the ileum in five separate areas. There were large lymph nodes throughout the mesentery. The liver was normal. Gross appearance of the lesion suggested an adenocarcinoma. An extended right hemicolectomy with removal of 60 cm. of the involved terminal ileum was done. Intestinal continuity was restored by an end-to-end ileotransverse colostomy. A biopsy of the anal lesion was done.

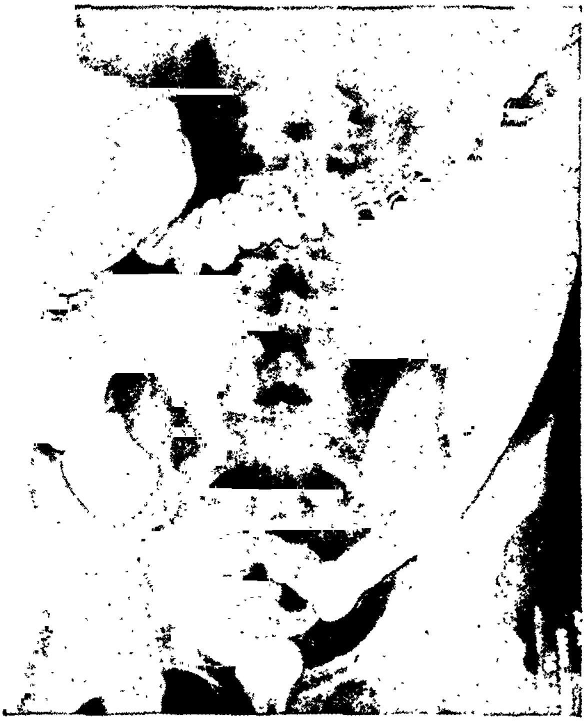

Fig. 1.—Roentgenographic study of colon, showing filling defect in ascending colon.

From the Ferguson-Droste-Ferguson Clinic.

The opened gross specimen had the appearance of a granulomatous disease rather than carcinoma. Microscopic sections (fig. 3) showed the lesion of the ileocecal region to be composed of multiple tuberculoid areas with groups of Langhans'-type giant cells. Some of the larger lesions contained areas of caseous necrosis. The anal ulcer revealed a chronic nonspecific inflammatory reaction. Special stains of the intestinal lesion showed rare acid-fast organisms suggestive of tubercle bacilli. Tubercle bacilli were identified on direct smear and culture of the sputum and gastric contents postoperatively.

When this was known the chest roentgenogram was reinterpreted as showing probable active pulmonary tuberculosis. Confronted with the diagnosis, the patient admitted that his mother and a sister had died of pulmonary tuberculosis. He had withheld this information because of the stigma he associated with the disease. After an uneventful recovery he was started on medical therapy and transferred to an appropriate facility.

Comment

It is our practice to obtain roentgenographic examination of the colon with barium enema on all patients admitted to the hospital for anorectal surgery. Benjamin and Todd[1] recently reported a series of 8,420 patients, from this clinic, in which x-ray studies of the colon with use of barium enema were done, after careful examination had failed to provide grounds for a diagnosis of colonic disease. Twelve per cent had disease of the colon which had been unsuspected previously. There were no cases of tuberculous enteritis in their series. Our own case is most unusual in that far-advanced tuberculosis of the intestine was discovered in an apparently well patient.

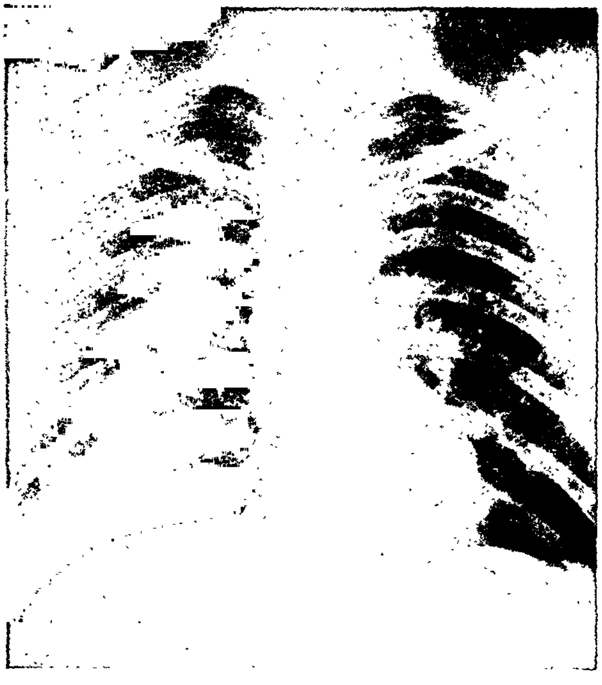
Fig. 2.—Roentgenogram of chest, originally interpreted as showing inactive pulmonary tuberculosis.

It is reasonable to assume that this patient was certainly approaching the development of symptoms, both pulmonary and abdominal. When seen for the first time he was still asymptomatic, except for a skin ulcer near the anus. The original interpretation of the one chest roentgenogram was somewhat misleading. A reliable family history would have resulted in more suspicion and a more intensive preoperative evaluation of the pulmonary system. The diagnosis of active pulmonary tuberculosis may have been established. Roentgenographic study of the colon was, nonetheless, strongly suggestive of a neoplasm, and surgical exploration would have been undertaken regardless. The appearance of the lesion at operation was that of an adenocarcinoma, and a resection was performed. The treatment of tuberculous enteritis, when the diagnosis is without question, is medical.

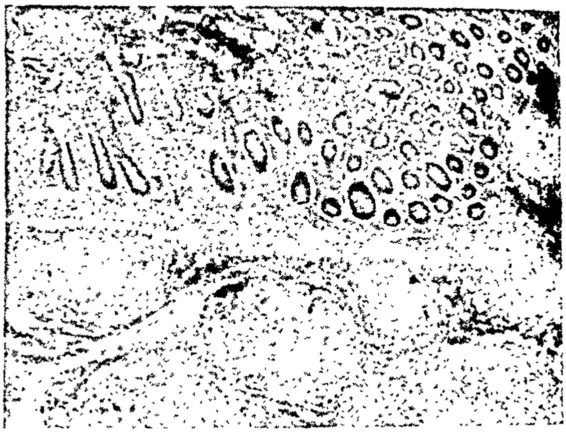
Fig. 3.—Microscopic section of intestinal lesion, showing typical tuberculoid areas with giant cell reaction.

Summary

A case of tuberculous enteritis showed the value of routine roentgenographic examination of the colon in patients with anorectal disease. Tuberculosis of the ileocecal region secondary to active pulmonary disease, without gastrointestinal and pulmonary symptoms, is rare and may easily be mistaken for a neoplasm. When roentgenographic studies suggest malignant disease, surgical exploration is mandatory. The surgical therapy must then be guided by the gross appearance of the lesion and the judgment of the surgeon.

3710 E. Fifth Ave., Denver 6. (Dr. Waggener).

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CORNEAL ULCER DUE TO CANDIDA PARAPSILOSIS (C. PARAKRUSEI)

P. Thomas Manchester Jr., M.D.
and
Lucille K. Georg, Ph.D., Atlanta, Ga.

A patient with superficial punctate keratitis, who was receiving antibiotic and steroid therapy, developed an indolent corneal ulcer due to Candida parapsilosis (C. parakrusei). Treatment, which included use of the antifungal antibiotics nystatin (Mycostatin) and amphotericin B (Fungizone), was followed by slow healing of the ulcer.

Report of a Case

The patient was first seen on Oct. 26, 1956, at the age of 37 years. She gave a history of five-year chronic recurrent inflammation of first one eye and then the other. Examination revealed a superficial punctate keratitis of the left eye. The vision was 20/20 in the right eye and only 2/200 in the left. The left eye was amblyopic due to esotropia in childhood. A litmus paper test revealed only 5 mm. of paper to be moist in the right side and only 6 mm. on the left after five minutes. The patient was thought to have keratitis sicca, and methylcellulose eye drops were prescribed to be used every two hours. She did not keep her appointments for follow-up examinations.

The patient was not seen again until Jan. 21, 1958, at which time she was found to have a small central corneal ulcer of the right eye which had been present for approximately 24 hours. A drop of 1% atropine solution was instilled and a patch was applied. When she returned the next day, the ulcer seemed worse. Sulfamethizole (Thiosulfil) was prescribed to be used every two hours; drops of 1% atropine solution were to be instilled morning and night. She was also to take 250 mg. of chloramphenicol (Chloromycetin) orally every six hours.

The corneal ulcer showed little improvement during the next five days, but the chloramphenicol dosage was stopped after the fifth day. Methylcellulose was instilled in both eyes every two hours. In addition, she was given therapeutic doses of vitamin A and vitamin B complex. On March 2, 1958, the eye became painful and an early trace of hypopyon was visible below. The patient refused hospital admission. Routine aerobic and anaerobic cultures revealed no growth of bacteria. Therapy with chloramphenicol was started again, 250 mg. four times daily. In addition, local treatment consisted of drops of tetracycline (Achromycin) solution every two hours and atropine three times a day. The treatment was continued for seven days with no improvement of the ulcer; on the contrary, the hypopyon had increased.

For several weeks the ulcer remained extremely indolent and essentially painless. The eye was not markedly inflamed, although there was a faint aqueous flare several weeks before the hypopyon developed. The ulcer, when stained with fluorescin, had a brownish color, but there was never a marked clouding of the cornea. The center of the ulcer was actually slightly raised and the general appearance suggested keratomalacia. It was approximately 3 mm. in diameter and extended downward only to the outer third of the corneal stroma. At this time a fungus infection was suspected.

Laboratory tests were made at the mycology unit of the Communicable Disease Center to determine whether the ulcer might be due to a fungus. The ulcer was rubbed with a sterile bacteriological loop and material was obtained for direct examination and culture. Wet preparations and stained smears revealed no bacterial or fungal elements. Cultures on Sabouraud dextrose agar with and without antibiotics (chloramphenicol, 0.05 mg. per milliliter, and cycloheximide, 0.5 mg. per milliliter) as well as brain-heart infusion agar were incubated at 25 C, and a similar set of cultures were incubated at 37 C. No growth was apparent for the first 10 days of incubation; however, after this time small white colonies were noted on the plain Sabouraud dextrose agar incubated at 25 C. Direct examination revealed them to be composed of small yeast-like cells. Their slow development and the small number of colonies made it difficult to determine whether this yeast-like organism could be the etiological agent or whether it represented a chance contaminant. Studies were undertaken to determine its identity.

The patient now agreed to hospital admission. Her physical examination showed nothing remarkable. Findings of routine blood studies and urinalysis were normal. Fasting blood vitamin A level was 130 mg. per 100 ml. She was taken to the operating room and the lacrimal puncta were severed and cauterized because of the bilateral tendency to keratitis sicca. A thorough débridement was per-

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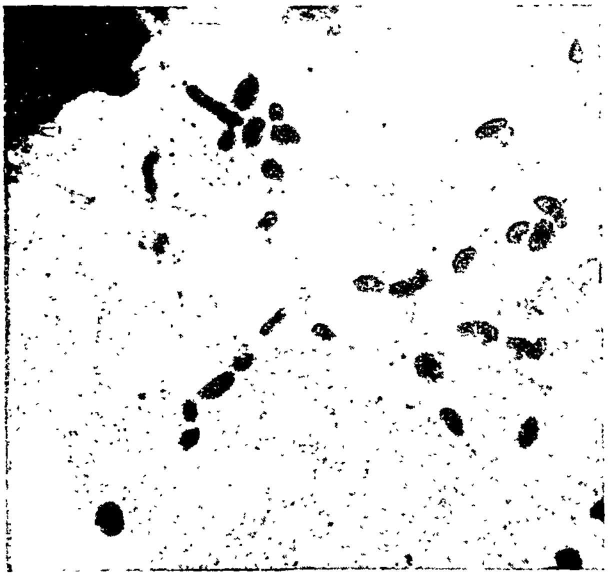
From the Department of Ophthalmology, Emory University School of Medicine; the Grady Clay Eye Clinic, Grady Memorial Hospital; Atlanta; and the Communicable Disease Center, Public Health Service, U. S. Department of Health, Education, and Welfare.

formed on the ulcer, and the corneal scrapings were used for smears and cultures. At this time the everted right upper tarsus had a white, frosted appearance. This area was also scraped for smears and cultures. Gram-stained smears now revealed large numbers of yeast-like budding cells. Some of the buds appeared elongate, suggesting the beginnings of mycelian formations (see figure). Yeast-like colonies developed within a few days on tubes of Sabouraud dextrose agar incubated at room temperature. These cultures, as well as the first obtained, were identified as Candida parapsilosis.

After it had been established that a fungus was the probable etiological agent, use of antibacterial antibiotics was stopped. Administration of atropine and methylcellulose was continued locally, and the patient was given orally 250 mg. of nystatin four times daily and six tablets daily of potassium iodine (Iodo-Niacin). In addition, a solution of amphotericin B was given in the form of eye drops, 1 mg. per milliliter every two hours. These drops seemed to burn and hurt the eye and their use was stopped after five days. During the first week of antifungal treatment the ulcer showed very little improvement.



Gram-stained smear from corneal ulcer, showing budding cells and beginnings of mycelian formations.

Cultures of the right eye on May 1, 1958, yielded a mixed growth of bacterial and yeast-like colonies. The eye at this time had become slightly more inflamed, and drops of 10% sulfacetamide (Sulamyd) solution were started four times daily. The bacterial culture was identified as Klebsiella species and the yeast-like culture as C. parapsilosis. On May 24, 1958, cultures revealed no growth of either bacteria or fungi, and it was noted that the eye was definitely better. Therefore use of sulfacetamide was continued locally. Drops of nystatin solution were also applied to the eye three times daily. Systemic administration of nystatin was continued for one month after the culture reports were negative. This medication did not cause the patient any pain. The ulcer was definitely smaller on May 31, 1958; and on June 18, 1958, the eye was white and did not stain with fluorescin. The vision still measured 2/200 because there was a deep corneal scar directly over the pupil. The patient was observed six months later and the lesion of the cornea had disappeared except for a thin scar, the eye appearing otherwise normal. The vision was now 20/50 in this eye.

Laboratory Identification of Candida Parapsilosis.—The organism was identified on the basis of its morphology on corn meal agar, its biochemical properties, and serologic reactions.

On corn meal agar cut plates the organism produced abundant mycelium and blastospores. The blastospores were single or in short chains. They were produced at the septa or distal ends of the mycelial cells. Both fine and coarse (giant form) mycelium were observed. The following sugars were fermented: dextrose with acid and gas and sucrose with acid only. Maltose and lactose were not fermented. Sugar assimilation tests showed positive utilization of dextrose, galactose, maltose, and sucrose. Lactose and raffinose were not utilized. Serologic identification was performed with use of monospecific antiserums homologous to antigens of the Candida species. Specific agglutination was obtained with those thermostable antigens which are unique to C. parapsilosis and C. pulcherrima. The latter species was eliminated as a possibility because of differences in morphology and biochemical reactions from the test organism.

Comment

Recent reports[1] have indicated that mycotic infections of the cornea are no longer rare, and there is considerable evidence that the use of antibiotics and steroids in the local management of acute ocular inflammation predisposes to invasion by fungi.

Experimental evidence that local use of cortisone and antibiotics facilitates fungus infections of the cornea has been provided by Ley.[2] This author demonstrated that cortisone, when applied to traumatized rabbit cornea in the presence of potentially pathogenic fungi, resulted in an 80% average incidence of infection, as contrasted with a 20% average incidence in the controls. The broad-spectrum antibiotic oxytetracycline, when combined with the inoculum, potentiated C. albicans infection of the immature rabbit's cornea.

Fungi which have been reported as causative agents in mycotic keratitis include both higher fungi and actinomycetes. Mikami and Stemmerman [1e] compiled a list from the literature comprising at least 13 genera. Some of these are fungi which are commonly thought of as pathogenic, such as Aspergillus fumigatus and C. albicans, but the large majority of reports concern fungi usually considered to be saprophytes.

It is important to point out, however, that the isolation of a fungus without demonstration of fungal elements in the tissues does not establish its causal relationship to the disease. In a number of recent reports, however, these criteria have been well satisfied. In other cases, although cultures have not been obtained, fungi have been clearly demonstrated in smears or stained tissue sections from diseased eyes. The table lists the cases of mycotic keratitis which have been proved on the basis of demonstration of fungi in the tissue, with or without cultural isolation of a fungous agent.

The factors which led to the infection in the case described are not known; however, it is known that the patient had been administering self-treatment for a period of two years for recurring episodes of eye inflammation, and it is believed that she used antibiotic and steroid eye drops for this purpose. When the ulcer appeared and the patient returned for treatment, antibiotics were used before its fungous etiology was suspected. There appears to be little question that the ulcer became steadily worse under this therapy. After the finding of yeast-like cells in smears the immediate withdrawal of these drugs and treatment with antifungal antibiotics resulted in a slow but steadily developing recovery.

Summary

A case of corneal ulcer was found to be due to Candida parapsilosis (C. parakrusei). It appears important that the clinician consider fungi in every case of hypopyon ulcer. The clinical and laboratory diagnosis of a corneal mycosis is important, for it demands immediate withdrawal of antibacterial antibiotics and corticoid preparations and institution of appropriate antifungal therapy.

Addendum

Since writing this paper we have learned of a report of three additional eye infections, two due to C. parapsilosis and one to Blastomyces species, published in the *Chinese Journal of Ophthalmology* (7:101-108, 1957).

Mycotic Infections of the Cornea

Year	Observer	No. of Cases	Fungal Agent Demonstrated in Tissue	Culture Obtained
1929	Wright, R. E.: Brit. J. Ophth. **13**:496, 1929	1	"Indistinct mycelium" reported	Glenospora graphii
1942	Bruce, G. M., and Locatcher-Khorazo, D.: Arch. Ophth. **27**:294, 1942	1	Gram-positive filaments	Nocardia
1944	Benedict, W. L., and Iverson, H. A.: Arch. Ophth. **32**:89, 1944	1	Not demonstrated*	Nocardia asteroides, 8 cultures over 4 yr.
1955	Mitsui and Hanabusa [1b]	1	Yeast-like cells	Candida albicans
		2	Mycelian elements	Aspergillus fumigatus
		1	Mycelian elements	Penicillium
1955	Pautler, E. E., and others: A. M. A. Arch. Ophth. **53**:385, 1955	1	Mycelian elements	Monosporium apiospermum
1956	Ley and Sanders [1c]	3	Mycelian elements	....
1956	Schardt, W. M., and others: Am. J. Ophth. **42**:303, 1956	1	Not demonstrated*	N. asteroides on repeat cultures
1957	Roberts [1d]	1	Yeast-like cells	C. albicans
1958	Gordon, M. A.: Personal communication	1	Mycelium	Allescheria boydii
1958	Haggerty and Zimmerman [1e]	14	Mycelian elements	....
		2	Yeast-like cells	....
1958	Mikami and Stemmerman [1a]	1	Mycelian elements	Fusarium oxysporum
1958	Present case	1	Yeast-like cells	C. parapsilosis

*Although fungal elements were not demonstrated in the tissues, these cases were included because a pathogenic fungus was repeatedly isolated from the lesions.

Dr. Takeshi Tsuchiya, of the Department of Bacteriology, School of Medicine, Juntendo University, Tokyo, Japan, performed the serologic identification tests.

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NUTMEG POISONING

Robert C. Green Jr., M.D., Winchester, Va.

The present-day use of nutmeg (Myristica fragrans) is confined largely to exploitation of its properties as a flavoring agent. In the past it has been used medicinally as an aromatic stimulant, a carminative, and a narcotic. In England and India it has been used widely by the laity as an emmenagogue and an abortifacient, and from these uses came many reports of nutmeg poisoning in the early literature. During the last 50 years nutmeg poisoning has seldom been reported, and only limited information is available concerning the physiological and biochemical effects of this particular toxic state.

Review of the Literature

One of the earliest cases of nutmeg poisoning was recorded by de Lobel in 1576.[1] In 1832 Purkinje [2] dramatically illustrated the toxic effect of this kernel by consuming three nutmegs, producing a narcosis which progressed to stupor. In 1903 Wallace,[3] in a review of cases of nutmeg poisoning, reported 25 from the world literature. Although one of the patients concerned died,[4] the remaining 24 recovered promptly without residual effects. Since Wallace's review a limited number of cases of nutmeg poisoning have been noted in the literature.[5] These more recent reports are brief; the clinical descriptions are meager and laboratory studies are not included. It is apparent from these reports and those of Wallace that only limited observation of nutmeg poisoning is available. Therefore, it was felt that a detailed report of such a case from my experience would be of interest.

Report of a Case

A 28-year-old woman was admitted to the Community Memorial Hospital in South Hill, Va., in a semistuporous condition. The medical and psychiatric history up to this time had been normal. She had been married nine years and had experienced two uneventful pregnancies. At 10 p. m. on the night before admission to the hospital she had eaten 18.3 Gm. of finely ground nutmeg in an attempt to induce the menses, which had been delayed two days. She had slept soundly without disturbance until 5:30 a. m. the next day. At that time she had been awakened by a burning sensation in the lower part of the abdomen and an overwhelming feeling of impending death. She vomited once. Her legs felt as if they were asleep and she complained of feeling "funny all over." She had then become completely disoriented, with episodes of wild screaming and purposeless thrashing of the arms and legs. Coordination appeared absent. Interspersed with this disorientation were brief moments of lucidity during which she seemed to be aware of her surroundings. From the time of her awakening at 5:30 a. m. until 9:30 a. m., when she was seen by her local physician, there were three intervals of lucidity, each lasting about 10 minutes. The rest of this time she was delirious and in a state of excitement and agitation.

This patient was admitted to the hospital at 11:30 a. m., about 13 hours after she had taken the nutmeg. On admission she was in a semistupor. She could be aroused to talk, but would immediately return to the semistuporous condition. The skin was cool but not clammy. There was no cyanosis. Blood pressure initially was 100/50 mm. Hg, pulse rate 100 and respirations 24 per minute, and temperature 98 F (36.7 C). The pupils were small and reaction to light was not visible. The thorax was clear to auscultation, palpation, and percussion. The heart was not enlarged and there were no murmurs. The abdomen was not tender and the liver, spleen, and kidneys were not palpable. The extremity reflexes were absent. Pelvic examination revealed evidence of beginning menstrual flow. Results of rectal examination were negative. The erythrocyte count was 3,710,000 per cubic millimeter, and the hemoglobin value was 6.8 Gm. per 100 cc. The leukocyte count was 7,400 per cubic millimeter, with 87% segmented neutrophils and 13% lymphocytes. Results of serologic tests were negative. Specific gravity of the urine was 1.020; the hydrogen-ion concentration was acid. Albumin content of urine was graded 2+; there was neither sugar nor bile. The carbon dioxide–combining power was 14.9 mEq. per liter of plasma. The serum sodium content was 126 mEq. per liter and plasma chloride content, 108 mEq. per liter. The serum potassium concentration was 3.8 mEq. per liter. The value for serum nonprotein nitrogen was 47 mg. per 100 cc.

The patient remained in a semistupor for 12 hours after her admission. She then began to experience episodes of wild excitement, with loud screaming and manifestations of a fear of impending death. She continued to be subjected to episodes of excitement for two hours, during which time restraints were needed. For the remainder of the second day she was restless but essentially quiet. During the third and fourth days of hospitalization she slept much but complained constantly, while awake, of a generalized feeling of numbness and dizziness.

Laboratory investigation on the third day revealed the value for serum nonprotein nitrogen to be 36.5 mg. per 100 cc. The specific gravity of the

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From the Medical Service, Community Memorial Hospital, South Hill, Va.

urine was 1.020; the hydrogen-ion concentration was acid. There was no albumin, sugar, or bile in the urine. The result of the sulfobromophthalein tolerance test was 10.5% retention of dye in 30 minutes. The direct serum bilirubin content was 0.05 mg. per 100 cc.; total bilirubin was 0.35 mg. per 100 cc. The reaction of the cephalin flocculation test was graded negative. On the fourth day of hospitalization the result of a phenolsulfonphthalein test was recorded as 77% excretion of the dye in two hours. Urine obtained during this test had a specific gravity of 1.002; there was no sugar, albumin, or bile. Total serum proteins amounted to 6.1 Gm. per 100 cc., with 4.5 Gm. of albumin and 1.6 Gm. of globulin. The prothrombin time was recorded as 100%. A transthoracic procedure to obtain hepatic tissue for biopsy was done at this time. Microscopic sections of the tissue showed no evidence of fatty infiltration or hepatic cell necrosis.

On the fifth hospital day the patient complained of nausea, dizziness, and generalized numbness. At intervals throughout this day she became restless and noisy and frequently expressed a fear of imminent death. These symptoms persisted intermittently with decreasing frequency and intensity through the sixth day. Between these episodes she appeared essentially normal.

She was discharged on the seventh hospital day. Laboratory studies at that time revealed retention of sulfobromophthalein to be 8% in 30 minutes. The specific gravity of the urine was 1.024; there was a trace of albumin, but no sugar or bile. The hydrogen-ion concentration was acid. The direct serum bilirubin content was 0.15 mg. per 100 cc., and the total bilirubin was 0.95 per 100 cc.

The patient returned for follow-up studies 10 days after discharge. At that time the results obtained from a complete blood cell count; urinalysis; cephalin flocculation, sulfobromophthalein, and serum bilirubin tests; and determination of nonprotein nitrogen remained essentially unchanged from those recorded at previous procedures. She reported that she was without symptoms of any kind. Because of the limited information available concerning nutmeg poisoning no specific therapy was given in this case, except for intramuscular injections of promazine hydrochloride during periods of excitement.

Comment

On the basis of the data in this case and in those noted from the literature it is apparent that nutmeg taken in moderate quantities may produce a serious toxic state and possibly death. To obtain a clearer understanding of the problem the pharmacological and chemical features of nutmeg will be discussed, as well as the clinical syndrome resulting from ingestion of the substance in toxic amounts. Because of the almost total absence of interest in this subject in the recent literature all information concerning the properties of nutmeg have come from a limited number of early studies.

Pharmacological Aspects.—Wallace reported that the toxic factor of nutmeg is confined entirely to the volatile oil component. He administered this oil (0.4 grains [24 mg.] per kilogram of body weight) to cats by a stomach tube and produced a striking clinical response. Within 10 minutes he noted restlessness, excitement, and excessive salivation. These signs were followed by a period of quiet associated with incoordination and staggering. Mydriasis was usually noted at this time. The reflexes became weakened and a condition of semiconsciousness supervened, during which respiration was labored and feeble. In some animals unconsciousness deepened, respiration became labored and feeble, and death occurred 8 to 12 hours after ingestion of the oil. Usually, however, after the stage of unconsciousness had developed, gradual improvement occurred, and about 15 hours after the oil had been given the animal appeared to return to normal. This improvement generally was temporary; the animal then gradually weakened, and within 36 to 72 hours after administration of the oil coma developed and death followed. Autopsy of these animals consistently showed advanced fatty degeneration of the liver.

Dale[6] and Jurss,[7] with use of myristicin, a constituent of the volatile oil, were able to reproduce in animals symptoms identical to those caused by the administration of nutmeg or the volatile oil of nutmeg. They concluded that myristicin is the toxic factor in nutmeg. Autopsy of their animals showed changes in the liver similar to those described by Wallace.

Chemical Aspects.—Nutmeg is known to contain from 5 to 15% volatile oil, 25 to 40% fixed oil, and 5 to 15% ash. The rest is starch, fiber, and water.[8] Power and Solway,[9] in an analysis of this volatile oil, found that 4% was myristicin. The formula for myristicin is $C_{11}H_{12}O_3$, and it is 5-allyl-1-methoxy-2,3,-methylenedioxybenzene. Further analysis of the volatile oil revealed 80% to be dextrocamphene and dextropinene, with 8% dipentene. Also noted were small amounts of eugenol, iso-eugenol, linalool, borneol, terpineol, geraniol, and safrol. In addition, Power and Solway isolated limited amounts of free myristic acid and traces of esters of this and other fatty acids.

Clinical Aspects.—It is apparent from this case and those previously reported that nutmeg in doses of 5 Gm. or more will produce a characteristic clinical syndrome. From one to seven hours after the ingestion of nutmeg symptoms of a burning midabdominal pain, with or without vomiting, may occur. Restlessness, giddiness, and excitement may be noted. Frequently a fear of impending death is reported, and often there is the complaint of a sensation of a heavy weight on the chest. During the next 10 hours drowsiness progressing to stupor may develop. However, the patient can be aroused; if this is done, delirium and agitation ensue and the patient sinks again into stupor. Some patients may not manifest the early symptoms of toxicity but may display only the late narcotic effect. As a rule recovery is complete within 24 hours. However, large doses of nutmeg may prolong recovery, and periodic outbursts of excitement with delirium may continue for several days or more.

Significant physical findings may include a decrease in blood pressure, with cyanosis and shock. In addition, there may be rapid respiration, tachycardia, dilatation of the pupils, and decreased or absent peripheral reflexes. Several of the early reports suggest that some patients may exhibit, in addition to the usual symptoms and signs, an acute allergic response to nutmeg. This response is manifested by edema of the eyelids, with marked flushing and itching of the face. There also may be an elevation of temperature. These symptoms of an allergic reaction apparently subside quickly.

Some of the laboratory findings in the case I have reported are not entirely understood. Since previous studies did not contain laboratory reports, the chemical determinations recorded in the present case are difficult to evaluate. In this case acidosis was noted, with depression of the values for serum sodium and serum potassium. The serum chloride content was within the normal range.

On the basis of the experimental work on cats by Wallace, Dale, and Jurss it appeared that fatty degeneration of the liver was the end-result of toxic doses of the volatile oil or its derivative myristicin. However, in the case reported here serial studies of hepatic function as well as biopsy of tissue from the liver revealed no evidence of damage to that structure.

Studies of renal function revealed an initial slight elevation of the nonprotein nitrogen value, as well as albumin content of grade 2+, although the output of urine during the first 24 hours was normal. The value for nonprotein nitrogen returned to normal the next day, and a subsequent urinalysis disclosed occasional traces of albumin. It seems probable that in the case presented here nutmeg produced a transient toxic effect on the kidney.

Summary

The toxic factor of nutmeg is known to be myristicin, a constituent of the volatile oil of nutmeg. Nutmeg in doses of 5 Gm. or more produces a marked depressive action on the central nervous system, as well as a less prominent stimulating effect. The clinical course may be severe, with coma, shock, and acidosis as its main features.

117 W. Boscawen St.

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UNDERNUTRITION AND ENDOCRINE DISTURBANCES.—Most patients with this disease [anorexia nervosa] at one time or another are suspected of primary hypofunction of the pituitary or of the adrenal cortex. . . . It is now becoming well recognized that undernutrition itself may lead to multiple endocrine disturbances. Undernourished subjects may show evidence of underfunction of the pituitary, thyroid, gonads and adrenals; Selye cites undernutrition as cause of adrenal exhaustion in his general adaptation syndrome. The whole relationship of the nutritional status to the endocrine system has recently been reviewed by Kennedy and McCance, who point out that multiple endocrine, as well as psychic, disturbances may be mediated through a final common pathway in the hypothalamus. However that may be, hypofunction of any of the endocrine glands does not readily explain . . . body fluid abnormalities . . . [such as] retention of chloride, sodium and water, depletion of potassium and protein, or redistribution of hydrogen.—J. R. Elkinton and E. J. Huth, Body Fluid Abnormalities in Anorexia Nervosa and Undernutrition, *Metabolism: Clinical and Experimental,* July (Part 1), 1959.

SPECIAL ARTICLE

PRIMER ON THE RHEUMATIC DISEASES

PART II

Prepared by a Committee of the American Rheumatism Association

Degenerative Joint Disease (Osteoarthritis)

Degenerative joint disease is a progressive deterioration of diarthrodial joints, characterized by mechanical erosion of articular cartilage and overgrowth of bone at the joint margins. Although this common articular disorder has been variously named osteoarthritis, hypertrophic arthritis, senescent arthritis, arthritis deformans, and arthrosis, the term degenerative joint disease is more accurately descriptive of the pathological changes occurring within the involved joints. The term, however, implies a generalized involvement of the joints of an affected person which is frequently not found. It has had limited acceptance, and the simpler designation, osteoarthritis, is most commonly used.

Etiology.—All of the factors contributing to osteoarthritis are not known. The etiology, however, includes mechanical, dystrophic, and genetic elements. Postmortem studies indicate that the degenerative changes in the cartilage are the earliest anatomic abnormalities and that a correlation exists between the severity of such changes and advancing age, while deterioration of cartilage in the knee joint may be demonstrated in some persons at the end of the second decade of life and is present in 80 to 90% of those over 60 years of age. Furthermore, increased wear and tear through abnormal use of a joint is known to accelerate and enhance the tendency to degenerative changes. Nevertheless, osteoarthritis is typically not a generalized disease but one localized to certain portions of individual joints. This observation, as well as the fact that some persons, even in the latter decades of life, are spared, suggests that the condition is also influenced by processes other than those related to aging and attrition. The exact nature of these other factors, however, remains obscure. A clear-cut relationship between endocrine abnormalities and degenerative joint disease has not been established. Vascular disturbances, arteriosclerosis, and uratic deposits have not been encountered oftener than might be expected in an isolated group of persons of the same age. Focal infection apparently plays no part. Psychic trauma may increase the subjective symptoms but has not been proved to alter the course pathologically.

Articular degenerative phenomena are increased by a variety of functional and anatomic derangements which result in injury to the joint. These include direct trauma, intra-articular fractures, dislocations, penetrating wounds, tears of ligaments or cartilage, osteochondritis, infection, neuromuscular disease, congenital defects, and developmental disturbances. The degenerative joint disease resulting from such conditions is usually spoken of as "secondary osteoarthritis." It is, however, similar to "primary osteoarthritis" except in respect to the time and manner of onset.

Although unproved in other forms of osteoarthritis, a genetic factor seems related to the appearance of the disease in the terminal interphalangeal finger joints (Heberden's nodes). Thus, the incidence of the condition is twice as great in the maternal parent and three times as great in sisters of patients as in the general population. Heberden's nodes, therefore, have a sex-influenced genetic characteristic, dominant in women and recessive in men.

Pathology.—As osteoarthritis progresses, the anatomic changes reflect loss of the inherent ability of cartilage to withstand the abrasive and compressive action incident to normal function. It remains unsettled, however, whether the initial defect occurs in the chondrocytes, in the fibrous proteins, in the unformed elements of the matrix, or elsewhere. Microscopically, a variety of focal degenerative changes have been described in the early phases, including edema and swelling of cartilage cells and chondromucoid softening of the matrix. Subsequently, there is noted mechanical abrasion of the articular cartilage, with tangential flaking parallel to the surface and splitting or fraying perpendicular to it, these latter changes taking place along the lines of collagenous planes. The resultant replacement of the usual smooth, glistening, homogeneous articulating surface by a fine fringed margin is

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The Committee of the American Rheumatism Association consists of Drs. Darrell C. Crain, Washington, D. C., Chairman; Wallace Epstein, San Francisco; David Howell, Miami; Harry Margolis, Pittsburgh; Elbert Phelps, Washington, D. C.; William Rawls, New York; Edward Rosenberg, Chicago; J. Edwin Seegmiller, Bethesda, Md.; Lawrence Shulman, Baltimore; Leon Sokoloff, Bethesda, Md.; Harry Thompson, Tucson, Ariz.; and Elam Toone, Richmond, Va.

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spoken of as fibrillation. Local areas of fraying are followed by more extensive disintegration and desquamation, with eventual denudation of the underlying bone.

As this process is taking place within the cartilage, there is concurrent reactive hyperplasia of the adjacent bone. Proliferation of the subchondral connective tissue of the marrow spaces finally involves the subchondral plate in the deeper part of the cartilage. This is thereby invaded, destroyed, and replaced by fibrovascular tissue which becomes ossified to form new bone. Through the constant friction of continued use this reactive bone, which now forms the joint surface in such an area of erosion, becomes highly polished, grossly resembling ivory. It is then spoken of as being eburnated. Comparable processes of reactive bone production occurring at the margin of the articular cartilage give rise to large bony overgrowths, commonly referred to as marginal osteophytes, spurs, or areas of lipping. In the distal interphalangeal joints, however, osteophyte formation has been noted without appreciable concurrent articular damage. Synovitis is usually lacking in osteoarthritis except when minute fragments of joint detritus are displaced into the synovial tissue. Since degenerative joint disease occurs in the older age group a concurrent osteoporosis, either menopausal or senile, may be present, which in weight-bearing joints, particularly the knees, may lead to remolding of epiphysial bone.

Osteophytosis of the spine, often referred to as hypertrophic osteoarthritis of the spine, should probably be distinguished from osteoarthritis of the spinal diarthroses. These osteophytes are formed most commonly at the anterior lateral margins of the ends of vertebral bodies and result from degeneration of intervertebral disks and ossification of the tendon attachments of abnormally stressed muscles. They bear an uncertain correlation to degeneration of apophysial (diarthrodial) joints of the spine. True ankylosis does not occur; nevertheless, varying degrees of spinal rigidity may be brought about by localized osseous bridging at varying points.

Clinical Features.—Degenerative joint disease presents many interesting and puzzling clinical aspects. Although an occasional patient complains of widespread distress, with symptoms in numerous peripheral joints as well as the spine, the majority will localize their complaints to a single joint or at the most to several joints. Furthermore, extensive articular damage may be visible roentgenographically, without significant symptoms. Despite these facts, a fairly uniform clinical pattern can be observed, occurring with increased frequency as persons progress beyond the fourth decade of life. The early symptoms are usually insidious: mild stiffness and aching pain in and about the affected joints, frequently associated with inclement weather. This may persist for many months or years, gradually increasing, with various degrees of severity; in some patients the symptoms remain relatively mild, while other patients become totally disabled. Severe changes occur most commonly in the weight-bearing joints. Physical signs in joints accessible to palpation are minimal soft tissue thickening, crepitus, and changes in the size and shape of the bone as the disease progresses. Effusions are noted only after trauma. In joints not accessible to palpation, such as the hips and spine, the only physical signs are loss of motion and pains on extremes of motion and at times muscle spasm. Constitutional signs incident to the disease are absent; nevertheless, those coincident with advancing years, such as weakness, fatigability, and general senile deterioration, may form an important part of the patient's complaints. In general, pain is more frequent in joints subject to strain, such as the lower part of the spine, hips, and knees, and the severity and nature of discomfort will usually relate to physical activity and the degree of mechanical derangement.

Although any diarthrodial articulation may be involved, some are more susceptible to degenerative changes than others, and symptoms may be influenced by the locality of the involvement. In the hands, the terminal interphalangeal finger joints are most frequently affected. Here, the nodular enlargements at the medial and lateral aspects of the dorsal surface are spoken of as Heberden's nodes. They are more frequent in women than in men, and of concern to the patient chiefly because of the unsightly character of the node rather than because of pain involved. At times, however, an inflammatory period may be present, usually of undetermined cause but at times due to either physical or psychic trauma. Osteoarthritic changes are also seen in the proximal interphalangeal joints and at the carpal-metacarpal articulations of the thumbs. The wrists, elbows, and shoulders rarely have symptomatic involvement and, when present, this is usually associated with occupational stresses or mechanical derangement. A severe form of degenerative joint disease is seen in the hips and is referred to as malum coxae senilis. Inflammatory stages are also recognized in this condition and the progressive nature of the hip involvement makes it a most painful form of the disease and refractory to treatment. Osteoarthritis of the cervical spine is frequently accompanied by degeneration and protrusion of intervertebral disks, at times with radicular symptoms noted in the upper extremities. In the lower part of the spine it is a common cause of persistent backache.

Degenerative joint disease usually pursues a slowly progressive but often intermittent course over many years. While it is not subject to the characteristic exacerbations and remissions of rheumatoid arthritis, periods of improvement, particularly under proper medical management, are frequent, being followed by other periods of symptomatic deterioration or acute episodes related to physical trauma or emotional upset.

Recently it has been postulated that a special form of osteoarthritis can be distinguished from degenerative joint disease and local osteoarthritis. This is spoken of as "primary generalized osteoarthritis" and is characterized by painful episodes affecting multiple joints usually in succession and lasting several months. Inflammatory signs as well as painful symptoms are observed in the distal and proximal interphalangeal joints and in the greater multangular–first metacarpal articulation. Other joints, however, particularly the knees, ankles, and spinal articulations, may be involved. Women are affected 10 times as frequently as men; symptoms are usually worse at night. Despite the fact that symptoms appear in multiple articulations and inflammatory signs may be present, the general health of the patient remains good and there is no sign of systemic disease except for an occasional elevation of the sedimentation rate. Differentiation from rheumatoid arthritis may be difficult. Roengenography is helpful, since severe osteophytosis is usually seen.

Laboratory and Roentgenologic Observations.—Degenerative joint disease has no characteristic laboratory manifestations. The sedimentation rate may be moderately elevated but is usually normal. Synovial fluid, when present in sufficient quantity for aspiration, has few abnormalities. The total white blood cell count and percentage of polymorphonuclear leukocytes are low.

Roentgenograms reveal narrowing of the joint space, with condensation of bone in the region of the articular cortex and irregular new growths of bone at the articular margins (osteophytes, spurs, and lipping). Discrete subchondral rarefactions (cysts) that sometimes resemble those of gouty arthritis may be present. Bone atrophy of a mild degree is not unusual, but if severe this suggests an associated disease.

Diagnosis.—On clinical examination this disease is not always obvious in the early stages. The presence of articular discomfort in the absence of clear-cut degenerative changes in the joint creates a difficult problem in differential diagnosis. In such instances other causes of skeletal discomfort must be carefully excluded. Intermittently progressive articular aching, relieved by rest and with minimal physical signs of joint disease, in a middle-aged person without evidence of general illness, should lead one to consider the diagnosis. Advanced degenerative joint disease is distinctive, especially when it affects the smaller finger joints, with firm, knobby enlargement leading eventually to deformities and a somewhat limited range of motion. One must be cautious in attributing skeletal symptoms to degenerative changes in the joints, particularly in the spine; and one must avoid misdiagnosis of superimposed disease such as metastatic malignancy, osteoporosis, and intercurrent infections. It is important to remember that the sudden onset of symptoms in previously asymptomatic joints requires an explanation. Degenerative lesions of the spine, especially in the cervical area, may produce symptoms in remote parts of the body.

When the two diseases are present in their classic forms, osteoarthritis and rheumatoid arthritis are dissimilar and should not be confused. Inasmuch as the onset of rheumatoid arthritis not infrequently occurs in later decades, when degenerative changes are common, the two diseases may coexist. If degenerative joint disease involves not only the terminal interphalangeal joints of the fingers (Heberden's nodes) but also the proximal ones, the deformities of the latter may simulate the fusiform swelling of rheumatoid arthritis. The hard, knobby character of the enlargement of degenerative joint disease and the absence of involvement in other joints as the disease progresses is a distinguishing feature. The presence of the "rheumatoid factor" in the serum of patients with rheumatoid arthritis may also be helpful.

Treatment.—Because of the degenerative character of the fundamental disorder, specific therapy does not exist. This form of rheumatism must be managed by the control of symptoms and relief of strains on the affected articulations. Except for degenerative hip or knee disease, which often ends in severe disability, and except for a small number of patients with an apparently marked constitutional predisposition, clinical results with this approach will be gratifying.

General: It is essential to alleviate the patient's fear of becoming helpless by imparting a proper perspective of his fundamentally benign disorder. It is unwise to imply that nothing can be done for him and that he need not return. In some patients coexistent neurotic conflicts and the attendant muscle tension appear to aggravate the disability. Resolution of emotional problems and the attainment of relaxation may produce striking benefits. Food intake should follow a normal pattern, unless caloric restrictions are advisable. Obesity is a common aggravating circumstance, and weight reduction is advisable to relieve abnormal strains on the joints of the lower part of the spine and the legs.

Rest: The most rational therapeutic measures are those combining general rest and individualized care for the affected part. The patient should be instructed to obtain at least eight hours of bed rest at night and, when possible, an additional afternoon rest period. When joints of the lower part of the spine, legs, and feet are involved, additional measures to relieve strain and weight-bearing may be necessary. Support to various parts can be provided by strapping, belts, braces, or the use of canes or crutches; additional rest in recumbency with or without traction may be required.

Physical Therapy: Physiatric measures are valuable in the treatment of degenerative joint disease and in the correction of improper posture that acts as a contributory factor. During especially painful phases such measures should be confined to applications of heat in a simple form, preferably hot soaks, hot towel packs, or infrared light, accompanied by stroking massage of the periarticular tissues and muscles. After a few days, when the lesion has become quiescent, passive motion should be added before a gradual return to active exercises and normal function. The benefit from roentgenologic therapy for the relief of pain is doubtful, and its use is unjustified when satisfactory relief can be obtained by safer means.

Drugs: Relief from pain and muscle spasm in this disease is usually afforded by therapy with the salicylates, particularly acetylsalicylic acid in doses of 0.6 to 0.9 Gm. three to five times daily. Phenylbutazone is occasionally used, but its administration must be carefully controlled because of its potential toxicity. The simultaneous administration of a mild sedative such as phenobarbital may be helpful in patients with significant nervous tension. Therapy with cortisone and corticotropin relieves symptoms in some patients but is not sufficiently effective to warrant routine use. Intra-articular administration of hydrocortisone in doses of 25 to 50 mg. affords temporary local amelioration of symptoms in most patients and can be a useful adjunct in the management of patients with excessively painful joints. Other glandular elements or vitamins should be given only when a definite deficiency can be demonstrated. Treatment with sex hormones has not proved effective.

Surgery: While the procedures outlined above may ordinarily be relied on to control symptoms and disability from degenerative joint disease, arthroplasty may sometimes be desirable or necessary in patients with badly deformed joints. Such a procedure is aimed at correcting mechanical disturbances and thereby improving motion and controlling pain. Débridement of joints, such as the knee, is occasionally resorted to for removal of hypertrophic bone and smoothing off of articular surfaces. Hip surgery in patients with malum coxae senilis has at times been more successful than surgery on other joints and may be a necessary approach to this particular problem when extensive changes occur. Several procedures are employed; a Vitallium cup over the head of the femur is most frequent, but varying portions of the neck or shaft can be replaced by acrylic or metal prostheses. None is universally satisfactory, and failures occur even when the procedures are performed by experienced surgeons.

Gout

Gout is a familial metabolic disease associated with abnormal amounts of urates in the body and characterized by an early stage of recurring acute monarticular arthritis and a late stage of chronic deforming arthritis, with varying constitutional symptoms. It occurs in all races, nationalities, and social levels. Approximately 95% of patients with gout are men, usually over the age of 30 years; in women the onset is usually after the menopause. From 3 to 5% of all cases of arthritis are probably gouty, although this diagnosis is frequently overlooked. The recognition of gout in one family member frequently leads to establishment of the diagnosis in others. Even more common than overt gout among members of such families is an elevated serum urate level (essential familial hyperuricemia).

Etiology.—The precise nature of the metabolic defect giving rise to the increased blood levels of uric acid in gout is not well understood. The genetic transmission of the trait for hyperuricemia has been attributed to a single dominant gene with incomplete penetrance which is not sex-linked, although recent studies suggest that the hyperuricemia may result from a multiple gene action.

The greatly expanded miscible pool of uric acid found in tophaceous gout demonstrates the dynamic equilibrium of urate deposits with the serum uric acid content. In human beings uric acid arises from two primary sources, the breakdown of dietary purines (the exogenous source) and the catabolism of tissue purines (the endogenous source). Studies of the incorporation of isotopically labeled glycine into uric acid have given evidence in a substantial portion of gouty patients of an excessive endogenous biosynthesis of uric acid direct from its simple and abundant precursors (glycine, CO_2 formyl groups, and the nitrogen of glutamine and aspartic acid), thus bypassing nucleic acid. No specific renal defect in the excretion of uric acid characteristic of gout has yet been demonstrated, although the generally diminished renal function in advanced stages of the disease undoubtedly contributes to urate retention. The precise relationship of hyperuricemia to acute gouty arthritis remains obscure; indeed, it seems possible that some other mechanism unrelated to the blood uric acid level may be responsible, since hyperuricemia not infrequently occurs without acute gouty arthritis.

Pathology.—The characteristic histological lesion of gout is the tophus, a nodular deposit composed of sodium acid urate crystals and the inflammatory foreign-body reaction they have evoked. In the joints, urates are deposited on the surface of the articular cartilage and also in synovial, capsular, and periarticular tissues, including subchondral marrow, periosteum, and tendons. The marrow deposits communicate with the joint space and constitute the so-called punched-out lesions seen in the roentgenograms. The pathological changes in acute gouty arthritis are not known with certainty, but some recent studies have indicated that urates are present in the synovial tissues in this phase. The chronically affected joint is predisposed to undergo osteoarthritic degeneration, and the joint at times is obliterated by massive tophaceous involvement. Arteriolar nephrosclerosis is commonly found in long-standing cases of gout, while the term gout nephrosis refers to the formation of microtophaceous deposits in the renal pyramids.

Clinical Course.—Individual patients exhibit a wide range of variation in the degree to which their gout is manifest. Some will show throughout life only the features of the disease usually associated with its early stages, consisting of a modest hyperuricemia and infrequently acute episodes of arthritis (acute gouty arthritis). Such attacks, which are self-limiting, subside spontaneously in 4 to 10 days or will respond within 24 to 36 hours to treatment with colchicine and leave no residual effects (intercritical gout). Patients at the other extreme, however, show the full course of the disease, consisting of (1) attacks of acute gouty arthritis recurring at progressively more frequent intervals over the years, (2) markedly elevated serum urate levels, (3) appearance of tophaceous deposits of sodium urate (tophaceous gout) in periarticular and subcutaneous tissues, cartilage, tendon, bone, kidney, and urinary tract, and (4) the eventual progression of the disease through the growth of these tophaceous deposits to a chronic deforming arthritis (chronic tophaceous gout) quite distinct in both pathogenesis and therapy from acute gouty arthritis. In addition, uric acid renal lithiasis occurs in 10 to 20% of gouty patients, and after years of gout renal dysfunction and a tendency to vascular sclerosis may develop.

The acute attacks are provoked by a variety of factors. Among these are such stress-producing events as surgery, trauma, systemic infections, allergens, and emotional disturbances, as well as dietary factors of excessive intake of nitrogenous or fatty foods, ingestion of alcohol, or a weight-reduction diet. Administration of liver extracts, vitamin B-complex, ergotamine tartrate, antibiotics, and mercurial diuretics may also provoke attacks.

Prodromal symptoms may be absent or nonspecific. The onset is characteristically sudden, with complete incapacitation from pain within 12 to 48 hours after the first warning twinge. In a typical case the joint area is warm, red, swollen, exquisitely tender, and excruciatingly painful to move. Bursal effusions, a moderate temperature elevation, leukocytosis, and an increased sedimentation rate may be present. The first metatarsophalangeal joint of the great toe is the first joint to be involved in approximately 25% of cases and will be involved in the early attacks of at least 90% of all cases (so-called podagra). All other large peripheral joints with the exception of the hips and shoulders may be affected. In the early stage the disease is almost always monarticular, but it becomes migratory and polyarticular with recurring attacks.

It is seldom symmetrical. Early untreated attacks usually subside within a week, and the persistence of symptoms more than 14 days in early cases raises a doubt as to the diagnosis. If proper treatment is instituted promptly, symptoms usually subside rapidly; if treatment is delayed, the response is less dramatic and recovery less rapid. Joint recovery is complete and the patient may remain free from symptoms for months or years. Subsequent attacks, however, occur at increasingly frequent intervals and eventually the acute attack will not subside entirely, gradually passing into chronic gouty arthritis associated with tophaceous deposits. This stage of the disease usually follows 10 or more years after the initial gouty attack.

Typical acute gouty arthritis may on occasions accompany blood dyscrasias, such as polycythemia vera, chronic leukemia, myeloid metaplasia, and multiple myeloma, and occasionally constitutes the presenting symptoms. Although referred to as "secondary gout" it is in all clinical respects similar to the "primary" variety, with the exception that a family history of gout is usually lacking.

Laboratory Observations.—An elevation in the serum urate concentration above 6 mg. per 100 ml. in males or 5.5 mg. per 100 ml. in females is found in over 95% of gouty patients and is a useful aid in the clinical diagnosis of gout. A simultaneous determination of blood urea nitrogen level and a complete blood count aid in distinguishing the hyperuricemia of gout from that of renal dysfunction and hematological disorders. In the evaluation of serum urate levels due consideration must be given to the uricosuric action of the antirheumatic drugs, including probenecid (Benemid), ACTH, steroid hormones and phenylbutazone (Butazolidin), and zoxazolamine (Flexin). Although salicylates in doses over 4 or 5 Gm. per day will exert a uricosuric action, they have been found to promote urate retention when given in doses of 3 Gm. per day.

Roentgenologic Examination.—Early in the course of gout, no abnormality can be detected by roentgenographic examination. However, with progression of the disease, tophi are observed as soft tissue swellings around affected joints and as punched-out radiolucent areas of epiphysial bone, particularly in the fingers and toes. In extreme cases this may produce marked erosion and destruction of the bone.

Diagnosis.—The excellent prognosis for most patients with gout, made possible by uricosuric agents, increases the importance of establishing the diagnosis at an early stage in the disease. The possibility of gout should be considered for any male over the age of 30 years having a first attack of arthritis. The characteristic abrupt onset and other clinical manifestations previously described, coupled with a family history of gout or renal calculi, lend additional support to the presumption of gout. The diagnosis can be confirmed by demonstration of an elevated serum urate level and by obtaining a prompt and complete response of the arthritis to a therapeutic test with colchicine. Acute gouty arthritis is often confused with acute pyogenic arthritis, cellulitis, rheumatic fever, calcific tendinitis, and occasionally rheumatoid arthritis. The diagnosis can be established conclusively in the tophaceous stage of the disease by the demonstration of urate crystals in the contents of a suspected tophus, by either microscopic examination or Weidel's murexide test. Such tophi are found most often about the margin of the ears, in the feet, the hands, and in the olecranon and prepatellar bursae. To establish the diagnosis in difficult cases urate crystals may be demonstrated in synovial tissue obtained at biopsy and fixed in absolute alcohol.

Treatment.—Relief of the presenting acute attack of gouty arthritis should be followed by a carefully individualized program of control to match the severity or stage of the disease.

Acute Gouty Arthritis.—During the acute attack the involved joint should be kept at rest. Local measures for pain relief depend on the patient's preference; use of narcotics may be justified. Once the acute symptoms disappear early ambulation and use of the joint should be encouraged.

Colchicine: Colchicine remains the preferred drug for relief of acute attacks of gout. One 0.5-mg. or 0.6-mg. tablet should be given each hour until either the joint symptoms are relieved or toxicity, manifested by nausea, vomiting, or diarrhea, appears. The diarrhea caused by colchicine often requires treatment with paregoric, 4 ml., or kaolin pectate, 30 ml., given after each loose stool. From 6 to 10 mg. of colchicine is usually required to produce such toxicity, but a therapeutic response is often possible with smaller amounts, especially if the drug is started early in the attack. Patients readily learn to abort many attacks by taking colchicine at the first premonitory symptom. Those who experience more than one or two attacks yearly may be started on therapy with 0.6 mg. of colchicine one to three times daily as a prophylactic regimen for reducing the frequency and severity of attacks.

Attacks can be rapidly terminated by administration of colchicine intravenously in a dose of 2 mg. with a repeat dose of 1 to 2 mg. in six hours, if there has been no response. No more than 5 mg. should be used for treatment of any single attack. Fewer gastrointestinal toxic effects accompany the use of colchicine intravenously, but absence of such warning symptoms could increase the hazard of accidental overdose.

Corticotropin (ACTH): Corticotropin is highly effective in rapidly terminating most acute attacks. It is especially useful in severe attacks and in attacks treated late in their course. A single intramuscular injection of 100 units of long-acting ACTH in repository gel or zinc form will usually result in relief of pain and swelling within several hours. Only rarely is a second injection of ACTH required, but administration of 1.2 to 1.8 mg. daily of colchicine for one to two weeks is necessary to prevent an early recurrence.

Phenylbutazone: Phenylbutazone is an effective agent for producing prompt relief of symptoms of acute gout, usually within 24 hours. It is particularly useful in terminating stubborn cases in which patients have not fully responded to colchicine or ACTH therapy. The initial dose of 400 mg. is given orally, followed by 100 or 200 mg. four times daily for two to three days. After this 1.2 to 1.8 mg. of colchicine is given daily for one to two weeks. Although the potential toxicity of phenylbutazone limits its routine use in gout, complications are rare when its administration is limited to the period indicated. Furthermore, the unpleasant gastrointestinal symptoms which accompany the use of colchicine are not observed. Because of this, many observers prefer phenylbutazone to colchicine in the treatment of acute gouty arthritis.

Steroid Hormones: Although some patients experience improvement from the administration of antirheumatic steroid hormones, the response is less consistent than with other methods of therapy. Their routine use in treating acute gout, or as maintenance therapy, is unwarranted.

Intra-articular Therapy: Hydrocortisone in a dose of 25 to 50 mg. injected intra-articularly into the involved joint is useful in the treatment of acute gout involving a single joint or bursa. Relief of pain is usually prompt and complete within 24 to 36 hours.

Interval and Chronic Tophaceous Gout.—Joint disabilities resulting from tophaceous deposits can be prevented, and to some degree reversed, through the mobilization of urate deposits with prolonged use of a uricosuric agent. Probenecid produces a marked increase in the excretion of uric acid and a drop in the serum urate level. Probenecid should be started at a dose of 0.5 Gm. per day with a fluid intake of at least 3 liters. Alkalinization of the urine to a pH above 6 by administering trisodium citrate, 1 teaspoonful four times per day, may be of help in preventing difficulties from urate calculi, especially during the early stages of treatment. Over a period of weeks the dose of probenecid is gradually increased to that required to maintain the serum urate at normal or near-normal levels, usually 1 to 2 Gm. per day. Use of salicylates tends to interfere with the action of probenecid and should be avoided. In the presence of severe renal disease the degree of uricosuria provided by probenecid is often inadequate and more potent drugs are needed to reduce the serum urate level to the normal range. Side-effects of gastrointestinal symptoms or skin eruptions occur in a small proportion of patients receiving probenecid and are an indication for use of a different uricosuric agent. A greater uricosuric action is provided by high doses of sodium salicylates (4 to 6 Gm. per day), but the symptoms of salicylism which frequently accompany this dosage are not well tolerated by most patients. Zoxazolamine and sulfinpyrazone (Anturan) are both highly potent uricosuric agents. Used together they have an additive effect. However, the increased potency carries with it the added hazard of precipitating urate calculi in the urinary tract, especially during the period of initiation of uricosuric therapy. This tendency of uric acid to deposit in the urinary tract can be reduced by a high fluid intake, alkalinization of the urine, and initiation of therapy with low doses of uricosuric agents. An initial dosage of 50 mg. twice daily of either zoxazolamine or sulfinpyrazone should be followed by a gradual increase in dosage over a period of one to two weeks until the desired serum urate levels have been achieved. Maintenance doses in the range of 200 to 400 mg. per day, given in four divided doses, are adequate for most patients. Daily administration of colchicine, 0.6 mg. three times a day, should be given when starting uricosuric therapy in order to suppress the acute attacks of gout that may be precipitated shortly after initiating such therapy. However, with continued uricosuric treatment the frequency of acute attacks is often reduced, and after many months of such therapy tophi may disappear or be arrested and the joint disability may be diminished.

Any one of the following features is indication for institution of therapy with a uricosuric agent in gouty subjects: (1) visual or roentgenologic evidence of tophi, (2) repeated serum urate levels above 8 mg.%, and (3) failure of maintenance therapy with colchicine to reduce the frequency or severity of attacks.

General Measures.—The primary purpose of a low-purine diet is to reduce the amount of uric acid produced by the body from exogenous purines and presented to the kidneys. The extent to which dietary restrictions are needed for control of the serum urate level will be highly individualized, determined by the severity of the manifestations of gout and the response to uricosuric agents.

All patients with gout should be given a well-balanced diet, eliminating such high-purine foods as liver, kidney, brains, sweetbreads, anchovies, sardines, beer, broth, meat soups, and leguminous vegetables. At the beginning of treatment other foods containing appreciable quantities of purines should be eaten sparingly, particularly meat and seafoods. These foods should be limited to 2 oz. (57 Gm.) twice a week, with the remainder of the dietary protein being made up of cheese, eggs, and dairy products. Liberalization of the diet with regard to the latter group of foods may be possible in the patient with tophaceous gout who shows a remarkable response to therapy with uricosuric agents, mobilization of tophi, and a serum urate level in the normal range. In the presence of severe tophaceous gout with marked impairment of renal function the protein content of the diet should be restricted to 50 to 70 Gm., since the endogenous production of purines is directly related to the nitrogen intake. Supplementary vitamins and minerals are of no value in the absence of a specific deficiency. Abundant fluids should be taken habitually to aid in the excretion of uric acid and prevent its precipitation in the urine as stones. The amount of alcohol permitted the gouty patient is a debatable subject. Excessive amounts should always be avoided, and, to be on the safe side, the gouty patient would do well to abstain entirely. In some cases, however, it may be better to permit an occasional drink rather than run the risk of periodic excess. Certain susceptible patients note acute symptoms after the ingestion of very small amounts.

Surgical excision of tophi is seldom indicated. Physical therapy and rehabilitation play as helpful a part in the treatment of gout as they do in the other rheumatic diseases. However, diathermy is seldom well tolerated. Because of the fact that surgery of any type may precipitate an acute attack the gouty patient, when being prepared for operation, should be placed on a purine-free diet for five days before and five days after operation and during that period given colchicine orally, 0.6 mg. three times a day. If an emergency operation is indicated, intravenous administration of colchicine the day of the operation will usually serve to abort an attack.

Collagen Diseases

The term "collagen diseases" is used to indicate several multisystem disorders grouped together because the characteristic pathological processes of each are found widely distributed in the collagenous connective tissues. Involvement of the joints is common. The cause of each disease within the group is unknown; a common etiology or pathogenesis has not been established. Nevertheless, two or more diseases may coexist in the same patient and, at times, symptoms of one may be succeeded by those of another. A common histological abnormality which forms an important characteristic of the group is referred to as "fibrinoid change."

This term refers to the affected tissues, which show a homogeneous, eosinophilic appearance having some of the tinctorial properties of the fibrin. The fibrinoid change may be seen either in the wall of blood vessels or in the connective tissue proper, and the materials responsible for its appearance are deposited in the interstitial matrix substance. Their composition varies, some containing fibrin and others gamma globulin. Systemic lupus erythematosus, polyarteritis nodosa, scleroderma, and dermatomyositis are the diseases usually included in this group. Although the pathological changes described also occur characteristically in patients with rheumatic fever and rheumatoid arthritis, these conditions have been considered separately.

Systemic Lupus Erythematosus

Systemic (disseminated) lupus erythematosus (SLE) is an apparently noninfectious inflammatory disease involving in large part the connective and vascular tissues of many organs and resulting in a variety of clinical manifestations secondary to the multiple system involvement. Although, as the name implies, tegumentary changes were originally regarded as a definitive aspect of the condition, this is no longer the case. The most common symptoms are those referable to the musculoskeletal system, but death ultimately results from visceral involvement. The disease usually runs a chronic course with remissions and exacerbations, periods of relatively good health being abruptly interrupted by explosive episodes. The disease usually begins in the third or fourth decade of life but may start in childhood or old age.

Etiology.—The cause is unknown, Although exposure to sunlight or ultraviolet rays, focal infection, reaction to foreign proteins or drugs, and emotional trauma have on occasions been identified with the onset of the disease or its exacerbations, none is consistently present. The occurrence of several abnormal serum proteins which react with a variety of nuclear fractions to bind complement suggests to many an autoimmune reaction, although such reactions are not definitive proof of their antibody nature. These and other serologic reactions will be discussed in more detail.

Pathology.—At autopsy gross findings are often minimal or absent and even in patients dying with highly active disease few specific histological lesions may be found. In various organs the connective tissue may reveal such nonspecific alterations as fibrinoid change and cellular infiltration, either within the walls of a blood vessel or outside of it. More characteristic changes include "atypical" verrucous endocarditis, disseminated arteritis, thickening of the basement membrane of a glomerular tuft ("wire loop" lesion), and periarterial concentric fibrosis of the spleen. "Hematoxylin bodies" (homogeneous purple masses of altered nuclear material identical with the inclusion body of the L. E. cell) represent the most characteristic histological finding of the disease but are not always present. The renal lesions may vary from focal glomerulitis to diffuse glomerulonephritis. Generalized lymphadenitis with infrequent areas of focal necrosis may be seen. Synovitis when present is of a nonspecific character but will occasionally manifest hematoxylin bodies.

Clinical Features.—Both the clinical picture at onset and the subsequent course are extremely variable. There is little difficulty in recognizing the disease in the patient with classic features of the acute, fulminating disease. These include high fever, symmetrical malar erythema ("butterfly rash"), severe joint and muscle pains, polyserositis, basilar pneumonitis, gallop rhythm, large lymph nodes, nephritis, psychosis or convulsions, and confirmatory laboratory findings. This form of the disease may cause death within a few weeks. In most cases, however, the course is chronic, lasting for years, active periods being interspersed with remissions of varying degree and duration. At the start a single organ system may be involved, with symptoms so vague that it is hard to date their onset. Thereafter, the disease may unfold in an episodic manner over several years. In other cases the onset of the disease may reflect acute involvement of several systems and later become chronic and remitting.

The joints are involved in approximately 90% of patients at one time or another. Arthritis is the initial manifestation in one-third of cases; it is present at onset along with other features in another third. Severe arthralgia, with little evidence of inflammation, is the usual picture, although a migratory polyarthritis involving usually hands, wrists, and knees, resembling rheumatic fever or rheumatoid arthritis, is also seen. Indeed, 30% of patients develop permanent clinically or roentgenologically visible evidence of arthritis, indistinguishable from that of rheumatoid arthritis. Severe deformities and subcutaneous nodules are also noted, but infrequently. Raynaud's phenomenon is not uncommon.

The cutaneous lesions also vary greatly. Most frequently these affect the face, neck, and extremities, especially the fingertips, and may be fleeting or chronic. Included are erythema, follicular plugging, atrophy, purpura, hyperpigmentation or vitiligo, angioneuritic edema, and alopecia. The relationship of discoid lupus erythematosus to the systemic disease is not clear. There are patients with SLE who first had the chronic discoid form for several years; other patients begin with the acute form and subsequently develop discoid lesions.

Half of the patients have local or generalized adenopathy. One-third have hepatomegaly, but jaundice is rare. The spleen is enlarged in only 15 to 20%. Pleurisy with or without effusion is noted in over half the cases and may be associated with an atelectatic pneumonitis, seen in 20%; a similar proportion have a complicating bacterial pneumonia. The heart is also involved in over one-half of the cases. Pericarditis is common, but large effusions are unusual. Myocarditis may lead to heart failure. Valvular lesions are only rarely associated with functional aberrations. Gastrointestinal symptoms include dysphagia, anorexia, nausea, vomiting, abdominal pain, diarrhea, and melena.

Renal involvement is a common and a serious feature of SLE. It begins as a focal glomerulitis, at which time urinalysis reveals only white blood cells; it may then pass through the nephrotic stage to the terminal picture of subacute glomerulonephritis with uremia and usually hypertension. Many patients exhibit neurotic or psychotic behavior, usually in a paranoid form, and some have convulsions. These reactions usually coincide with highly active disease and are ominous signs. Peripheral neuritis is rare. More than 25% of patients have retinal lesions. The most frequent finding is small white spots in the nerve fiber layer of the retina, called "cytoid bodies."

Laboratory Findings.—Anemia is found in 80% of cases. This is usually moderate and of the normochromic and normocytic variety. Severe hemolytic anemia, probably not due to hypersplenism, is found in 5% of cases. Some patients with SLE show antibodies against red blood cell antigens; but transfusion reactions are not excessive. Purpuric lesions are common. One of several factors is responsible: involvement of small vessels with SLE, azotemia, thrombocytopenia, or in rare instances a peculiar circulating anticoagulant or prothrombin deficiency secondary to liver disease. The white blood cell count is usually low normal or slightly subnormal. Extreme leukopenia is rare.

The erythrocyte sedimentation rate is elevated in almost all patients with active disease and may remain high in clinically apparent remissions. In half the cases there is an increase in the serum globulin concentration, usually in the gamma and alpha-2 fractions, and there are also positive cephalin-cholesterol flocculation and thymol turbidity reactions. Other evidences of plasma protein dysfunction include red blood cell autoagglutination, circulating anticoagulant, positive result of Coombs' test, cryoglobulinemia, lowered serum complement activity, the presence of the rheumatoid factor in up to 34%, and a chronic biological false-positive result of the serologic test for syphilis in 20% of cases.

Another important serologic reaction is the L. E. cell phenomenon which, if present, strengthens the diagnosis, with certain reservations. A typical L. E. cell is a polymorphonuclear leukocyte, largely filled with and enlarged by an inclusion body, a globular mass of homogeneous material appearing like ground glass and staining red-purple with Wright's stain. The same material may be observed extracellularly as free "globs" or "rosettes," i. e., globs surrounded by neutrophils. Three factors are essential for L. E. cell formation: (1) a serum factor, acting on (2) damaged leukocytic nuclei, and (3) phagocytic cells to engulf the altered nuclear material. The test is carried out in vitro and only *the serum factor must come from the patient with* SLE. It resides in the gamma globulin fraction. The reaction between L. E. factor and nuclear material is [illegible]

The [illegible] L. E. cell test results in patients with SLE is 69 to 100%, but such figures have limited significance, considering the lack of satisfactory criteria for the diagnosis of SLE. There are three interesting "false-positive" categories; the hydralazine syndrome, consisting of rheumatoid symptoms occurring in patients treated over long periods of time with hydralazine; various hepatic disorders; and other "collagen diseases" (in both rheumatoid arthritis and scleroderma the incidence of false-positive test results may approximate 15% or more of all cases). The correlation between the number of L. E. cells observed and the activity of SLE is poor.

Roentgenograms of the chest may reveal disk-like atelectases at the lung bases and cardiomegaly. The degree of renal involvement is reflected in the urinalysis, where albumin, red blood cells, and hyaline or granular casts may be found.

Diagnosis.—The patient with a classic clinical picture, compatible biopsy findings, and a positive L. E. cell test result poses no diagnostic problem. This, however, is not the usual mode of presentation. The disease generally unfolds in an episodic manner, and at the beginning, or even later, only one manifestation may be dominant. In such situations a careful history may disclose previous unexplained illness, or there may be concurrent atypical clinical, physical, or laboratory findings, evidence of protein dysfunction, or a positive L. E. cell test result. Punch biopsy of the kidney may be helpful in cases with renal involvement.

The differentiation between SLE and other rheumatic disorders may be difficult. An example is the "rheumatoid arthritic" who has fever, subcutaneous nodules, pericarditis, anemia, and L. E. cells. To some it would seem that this patient has severe rheumatoid arthritis and a false-positive L. E. cell test result; to others, that he has SLE with prominent joint involvement. This problem has not yet been resolved.

Prognosis.—The outcome may be death in a few weeks or a benign course lasting decades. The death rate after diagnosis is estimated to be constant at 10% per year.

Treatment.—Treatment with steroids may produce dramatic improvement but should be prescribed only for severe acute attacks or for significant involvement of a vital organ system. At such times administration in adequate doses may be lifesaving.

The amount of steroid necessary is usually considerably higher than that used in the control of rheumatoid arthritis. Thirty to forty milligrams of prednisone per day is an average dose, but some patients may require two or even three times this amount. The drug should be withdrawn as the acute exacerbation subsides.

Between attacks, or during exacerbations of modest severity, therapy with salicylates may lessen fever and joint pains. Otherwise, treatment is purely symptomatic. Synthetic antimalarial compounds such as chloroquine sulfate and dihydroxychloroquine phosphate apparently have a beneficial effect on some of the cutaneous lesions but are otherwise of questionable value. Patients should be advised to avoid exposure to the sun and should be cautioned about possible adverse drug reactions.

Polyarteritis (Periarteritis) Nodosa

Polyarteritis nodosa is an apparently noninfectious disease characterized by segmental inflammation of medium-sized or small arteries, with varying multisystem manifestations, depending on the site of arterial involvement. It may appear at any age but is most common in middle life; the incidence is greater in males.

Etiology.—The cause of the condition is unknown. Necrotizing arteritis similar to the human lesion can be produced in experimental animals by sensitization to foreign protein and by other means. Moreover, polyarteritis has been found in some patients dying of serum sickness or of apparent hypersensitivity to such drugs as sulfonamides, arsenicals, iodides, and penicillin. In the majority of cases, however, careful questioning fails to reveal evidence of sensitization. It is possible that a number of etiological agents and diverse pathogenic mechanisms may be involved in the development of the lesion.

Pathology.—Histologically, the active arterial lesions show segmental necrosis, fibrinoid change, and infiltration with leukocytes. Eosinophils may also be present but are not essential for the pathological diagnosis. Attempts at repair may result in complete healing, fibrosis of the adventitia producing the nodules (which may be detected clinically), or intimal proliferation together with thrombosis and infarction. These lesions may affect the entire circumference of a vessel or only a portion. Aneurysmal dilatation of the vessel wall may lead to its rupture. The usual picture at autopsy consists of vessels exhibiting various stages of inflammation and repair. No single set of vessels is found to be involved in every case. Any organ may be affected. Most frequently, however, the lesions are seen in the kidney, peripheral nerves, muscles, gastrointestinal tract, heart, and liver.

Some investigators divide the angiitides into several types, depending on histological features, distribution of lesions, and the associated clinical condition. It remains to be determined whether or not such divisions are justified.

Clinical Features.—Symptoms and signs are so protean that no typical description is possible. The onset may be acute or insidious. The disease may appear as (1) fever of unknown origin; (2) primary renal disease, thought to be glomerulonephritis; (3) severe abdominal pain, often with hematemesis or melena; (4) bronchial asthma or bronchopneumonia; (5) cardiac failure; (6) muscle pains and weight loss; or (7) painful peripheral neuritis, often bilateral.

It is usually a combination of features that suggests the correct diagnosis. Renal involvement is the most frequent. Hypertension is present in more than half the cases. Cutaneous manifestations may include erythematous eruptions, bullae, purpura, and subcutaneous nodules. Nodules have a linear distribution along the course of arteries. Arthralgias, polyneuritis, and myositis are common, but true arthritis is relatively rare.

Laboratory Findings.—Leukocytosis, with a shift to the left, is usually noted, although the white blood cell count may be normal or low. Eosinophilia is particularly apt to be present in patients with bronchial asthma. A mild normocytic anemia is common; severe anemia is usually the result of blood loss. Albuminuria and hematuria are the common urinary abnormalities, although white blood cells and casts may also be seen. The sedimentation rate is usually elevated and the serum globulin level is often elevated.

Diagnosis.—The correct diagnosis may be suggested by the clinical and laboratory findings, but biopsy remains the sole means of establishing it with certainty during life. Even so, only one-quarter to one-third of random biopsies done on patients later proved at autopsy to have the disease have been shown to be positive. Material for biopsy should be obtained from a painful area, if possible, and adequate (2 by 1 by 1 cm.) specimens of muscle are desired. Because of the segmental nature of the involvement serial or multiple sections may be necessary to demonstrate the lesion.

Arteritis similar to that observed in polyarteritis nodosa may also be found in rheumatoid arthritis, systemic lupus erythematosus, scleroderma, and, less frequently, rheumatic fever. The relationship between that found in polyarteritis nodosa and that found in rheumatoid arthritis has been discussed more fully under the latter disease.

"Wegener's granulomatosis" is characterized pathologically by necrotizing granulomatous lesions of the respiratory tract, generalized arteritis, and focal glomerulitis. Clinically, it begins with severe destructive sinusitis or rhinitis or persistent pneumonitis, followed by signs of renal damage and generalized vasculitis.

Prognosis.—The prognosis generally is poor, with death the usual outcome after weeks or months of illness. However, patients may live for years, enjoying good health, when vital organs are not severely involved.

Treatment.—No specific therapy is known. Although the number of cases responding favorably to treatment with steroid compounds is discouragingly small, a therapeutic trial is justified. Supportive measures may be of value. Every effort should be made to eliminate any potentially offending antigen.

Scleroderma

Scleroderma is a chronic disease characterized by fibrous thickening of the dermis and the connective tissue of various internal organs. Because viscera are often affected it is at times referred to as "progressive systemic sclerosis." It is not rare. The peak incidence is in persons between the ages of 30 and 50 years, although it may affect persons of any age; it is more frequent in women than men. The course is usually slowly progressive.

Etiology.—The etiology is obscure. There is no evidence to support the concept of hypersensitivity. The autonomic nervous system has been implicated by the frequency of Raynaud's phenomenon and the reported improvement after sympathectomy in some patients. The presence of a psychological component in most cases is of interest.

Pathology.—Early in the disease sections of the skin may appear normal. As the condition progresses the dermis is thickened by coarse collagen bundles lying parallel to the surface of the skin. This fibrous deposit frequently extends into the subjacent adipose tissues. Hyalinization may eventually occur, with loss of all skin appendages. Calcification in the skin is not uncommon. Fibrosis commonly occurs in other organs, including the alimentary tract, myocardium, lung parenchyma, and muscle.

Vascular lesions involving small arteries and arterioles are found in the majority of cases at autopsy. The kidney is the most frequent site. The lesion may be chronic, with marked intimal fibrosis, or it may be acute, with deposition of fibrin-like material beneath the endothelium. The latter may be associated with platelet thrombosis of arterioles and capillaries. Focal glomerular necrosis or cortical infarctions are present in many instances. Glomerulonephritis is not found. Chronic myositis and fibrinous synovitis are also common findings.

Clinical Features.—The onset is characteristically insidious. Stiffness of the fingers and hands may be an early complaint. Raynaud's phenomenon and hyperhidrosis of the palms and soles may antedate other manifestations by months or years. The earliest lesions of the skin are found usually in the hands or feet, less commonly in the face and neck. These consist of a diffuse, nonpitting edema, usually without erythema. The involved skin then becomes waxy, taut, hard, thickened, and finally bound firmly to the underlying structures. Normal skin folds disappear, producing a mask-like appearance in the face. The process may then spread centrally from the distal parts of the extremities and involve the entire integument. Brown pigmentation and vitiligo are common. The fingers may become immobilized in flexion. Ulcers, difficult to treat, appear on the fingertips and at pressure points over joints. Both diffuse subcutaneous calcifications (calcinosis universalis) and periarticular calcifications (calcinosis circumscripta) are seen. Recurrent polyarthritis is common but rarely leads to deformities.

Dysphagia and sour eructations due to esophageal involvement are common and may precede skin involvement. Small-intestinal disease may appear later, with symptoms suggesting obstruction or paralytic ileus.

Pulmonary symptoms, usually tachypnea and dyspnea, may result from sclerodermatous encasement of the thorax impeding respiratory motions or impairment of alveolar diffusion secondary to fibrosis of the lung parenchyma. Aspiration pneumonia may result from difficulty in deglutition. Involvement of the myocardium may cause arrhythmias, conduction defects, and heart failure. Renal involvement, with uremia and malignant hypertension, is a common terminal event.

Laboratory Findings.—Blood studies give normal results except during periods of active disease, at which times the erythrocyte sedimentation rate is elevated and the serum protein content altered, with a reversal of the normal albumin:globulin ratio. When renal involvement supervenes the urinalysis shows albuminuria, red blood cells, and casts. The serum calcium, phosphorus, and alkaline phosphatase activity are normal in the presence or absence of calcinosis. Roentgenograms of the involved parts may reveal osteoporosis, destruction of the distal phalanges, and subcutaneous or periarticular calcifications. The esophagus may be dilated and without normal peristaltic activity. The antrum of the stomach may be constricted and the small intestine segmentally dilated. Roentgenograms of the chest may reveal diffuse pulmonary fibrosis, occasionally with small cysts.

Diagnosis.—Dermal changes are characteristic in the well-developed cases and may be confirmed by biopsy. Early changes in the fingers may simulate those of rheumatoid arthritis or systemic lupus erythematosus. At times patients may appear with simultaneous clinical and laboratory characteristics of scleroderma, as well as rheumatoid arthritis, systemic lupus erythematosus, and dermatomyositis. Progressive systemic sclerosis should not be confused with "morphea," or localized scleroderma, in most cases of which there is no evidence of extracutaneous disease.

Prognosis.—A prolonged, progressive course of many years' duration is the rule. In some cases death results from renal involvement, with rapidly advancing malignant hypertension, or from pulmonary or cardiac dysfunction.

Treatment.—No specific remedies have proved to be of consistent value in the treatment of the disease. Physical therapeutic measures should be applied to combat contractures and preserve muscle strength. Sympathectomy usually fails to give more than transient relief, principally from the vasomotor phenomena.

Dermatomyositis

Dermatomyositis is an ill-defined disorder characterized primarily by chronic nonsuppurative inflammation of the skin and striated muscles. The term "polymyositis" is used when there is only muscle involvement. It may affect persons of any age; although it is most common in middle life, its incidence in children is appreciable. It is slightly more common in females.

Etiology.—The cause is unknown. However, the incidence of neoplastic disease in dermatomyositis is much greater than would be expected on the basis of chance alone, being reported in as many as 34% of adult cases. The tumors are of various types and from different primary sites. The relationship between the two conditions, however, remains a mystery, since symptoms of dermatomyositis frequently continue after successful therapy of the associated tumor.

Pathology.—Variable nonspecific patterns of dermatitis are seen. The muscles may grossly appear pale, with areas of yellow or pink patches of discoloration. Histological alterations in striated muscle include atrophy, necrosis, hyalinization, and fragmentation of the fibers; proliferation of sarcolemmic nuclei; and occasional scattered giant cells. Lymphocytes, plasma cells, and histiocytes are seen around small blood vessels or in other parts of the muscle. Multiple gastrointestinal ulcers occur with some frequency.

Clinical Features.—The onset may be explosive or insidious, with low-grade fever, weight loss, malaise, weakness, and muscle aching. Raynaud's phenomenon may be present. Edema of the face, particularly striking in the periorbital region, is associated with a purple-red (heliotrope) discoloration. The skin over the face and V-area of the neck may appear diffusely red or telangiectatic. The dermatitis elsewhere is quite variable. Mottled or diffuse erythema, with or without edema and often desquamating, is common on the extensor surfaces of the arms and legs as well as on the trunk. Later in the disease there may be patchy hyperpigmentation or subcutaneous calcification, with extrusion of calcific deposits through the skin.

The most important feature is the muscle involvement, which is manifested by aching, tenderness, weakness, and stiffness. Characteristically, the proximal muscle groups of the upper and lower extremities are more frequently and severely involved than the distal ones. Because of this, the patient may be unable to comb his hair or maintain a steady gait. With more severe involvement he is unable to sit up in bed or lift his head from the pillow. Initially the muscles may feel doughy and later, firm. With further progression they become atrophic and fibrotic, with contractures of shoulders, elbows, hips, and knees. Arthralgia may be an early complaint, but there is little, if any, arthritis.

Involvement of specialized muscles may produce such functional changes as palsies of extraocular muscles with diplopia, dysphagia, hoarseness, or ventilatory insufficiency. Ulcers of the alimentary tract may be encountered in patients with late cases.

Laboratory Findings.—The erythrocyte sedimentation rate is elevated during active periods. Slight anemia is common. The white blood cell count is usually normal, but there may be a transient eosinophilia or monocytosis. The serum globulin concentration may be modestly increased. As in other muscle-destroying diseases the urinary excretion of creatinine is reduced and that of creatine raised. The serum glutamic oxalacetic transaminase (SGO-T) level is usually elevated. The electromyographic changes are nonspecific. Roentgenologic examination may reveal extensive subcutaneous calcifications, which in some cases are concentrated periarticularly.

Diagnosis.—The diagnosis is made largely on the basis of the clinical picture and may be strengthened by compatible muscle or skin biopsy findings. Early in the disease, however, it may be difficult to distinguish dermatomyositis from progressive systemic sclerosis, scleredema, or systemic lupus erythematosus. When the cutaneous manifestations are absent or minimal, such muscle disorders as myasthenia gravis, progressive muscular dystrophy, or thyrotoxic myopathy must be excluded by specific laboratory tests for these disorders.

Prognosis.—Death is the outcome in about half the cases. Although the disease may be rapidly fulminating, the usual course is one of moderate progression. Those surviving the first year have an excellent prognosis for life but may be left with crippling muscular defects.

Treatment.—Therapy is largely symptomatic. Of all the agents tried, only the adrenocortical steroids offer any hope of combating the disorder. In most patients there is no response to therapy with steroids, but the occasional striking improvement warrants a full trial. Physical therapy may help to preserve maximal use of unaffected muscle and prevent contractures. In view of the supposed improvement in some cases after removal of a malignancy, a thorough search for tumor should be carried out.

COUNCIL ON DRUGS

Report to the Council

The Council has authorized publication of the following report.

H. D. KAUTZ, M.D., *Secretary.*

CURRENT STATUS OF THE THERAPY OF BURNS

Isidor S. Ravdin, M.D., Philadelphia

Many of the most important aspects of the therapy of burns have not changed to any significant degree in the last few years. The need for supportive therapy of a general character, gentleness in the handling of the patient, and exacting cleanliness in the handling of the burned patient are just as fundamental today as they were before the days of chemotherapy, of transfusion, and of fluid and electrolytes. These fundamental principles apply to the patient as a whole, as well as to the local wound. They, very likely, outweigh recent contributions which have been made in the care of the burned patient.

General Considerations

Significant strides have been made in the treatment of shock with the greater use of blood, plasma, and, at times, plasma expanders. Significant progress has been made in the prevention of electrolyte imbalance, its recognition, and correction. Septicemia, the greatest cause of death in the salvable burned patient, has been curtailed by the judicious use of antibiotics. It is important, however, to point out that the routine prophylactic use of systemically administered antibiotics is probably contraindicated except in the very severe burns. When antibiotics are indicated, they should be changed every few days to minimize the development of resistant strains of organisms. When staphylococcic infection occurs, the strains should be rapidly determined, and the antibiotics used should be those to which these strains are sensitive. The use of cortisone (Cortisone, Cortogen, Cortone) acetate and corticotropin (Acth, Acthar, Corticotropin) has been discontinued almost completely.

It should be pointed out that the careful use of specifically indicated antibiotics may be lifesaving in patients who have developed septicemia but that, in the local care of the burn wound, antibiotics have contributed very little. Surgical cleanliness in the care of the wound is more important than the use of antibiotics to control surface infection of the burned area, where infection has taken place because of inadequate cleanliness.

Specific Measures

Widespread claims have been made for a variety of locally applied agents concerning their ability to accelerate nature's processes of healing; however, the most exacting studies have failed to fulfill the claims made for any of these agents. After careful study, the innumerable substances which have been advocated for local use have proved to be of little practical value. In fact, many of the agents which have been used to promote healing have been shown to be detrimental to epithelization.

Enzymatic débriding agents have been advocated by several investigators, but, in spite of impressive laboratory work, they have not proved to be very effective in man. The best method of cleaning the burned area, if this is necessary, is still by washing with surgical soap and sterile water or physiological saline solution. The best débridement is still achieved by time or the surgeon's scalpel, and the best dressing is still a fine-mesh gauze lightly impregnated with an innocuous bland ointment.

The only worthwhile place for a specialized burn ointment (if such an ointment exists) seems to be on a small superficial burn for the immediate relief of pain. Even so, burn wounds are seen daily which have had no mechanical cleansing and which are badly infected, in spite of the generous application of some proprietary ointment. History has repeated itself over the centuries.

Clinical studies have shown clearly that, in third degree burns, rapid healing is best obtained if the granulating surface and surrounding skin are kept meticulously clean with soap and water, plus the frugal use of ether or benzene for the removal of keratin scales and macerated tissues. Skin grafting is faster than any known therapeutic agent in providing coverage for areas of deep burns, reducing the bacterial flora of a wound, and restoring the critically burned patient to good health. Frequent blood transfusions, light safe anesthesia, and nutritional adjuncts given intravenously or orally have added greatly in reaching this goal. The best means of providing adequate calories is by mouth. This method should always be used if possible. Intravenous alimentation should be used to increase oral caloric intake, if this is inadequate.

John Rhea Barton Professor of Surgery, Hospital of the University of Pennsylvania Department of Surgery.

Progress in the treatment of burn shock has been great, and, if it is treated early, the large majority of severely burned patients can now be brought successfully through this phase of their injury. Several formulas have been proposed as guides for the administration of fluid during the shock phase. At times, too much fluid is given, and pulmonary edema is produced. One cause of overhydration is overestimation of the area burned. Less than the estimated volume of fluid should be given to children, elderly patients, those with serious heart disease, those with respiratory burns, and those with more than 40% of burned body surface. Each patient's response must be closely observed and his therapy adjusted accordingly. The use of an indwelling catheter in the urinary bladder enables one to follow closely the rate of formation of urine and is helpful in judging the adequacy of intake. Urine formation of 25 to 50 cc. an hour is a satisfactory rate, but fluid therapy should not be gauged on this factor alone.

Contrary to the prevailing opinion of a decade ago, it is now believed that large quantities of salt may be necessary in the early phase of treatment because of the rapid fall in the level of serum sodium. Associated with the rapid drop in serum sodium, there is a period of sodium retention usually lasting several days. After the period of retention, the kidneys usually excrete a large amount of fluid and sodium, unless severe renal damage exists. If the salt solution can be given orally, a weaker solution not only is better tolerated but also obviates the necessity of giving the extra water intravenously. The more severely burned patients, however, often cannot tolerate fluids given by mouth.

The rapid loss of plasma from the burned surface and into the tissue beneath the burn has long been recognized, and, until recent years, plasma alone has been considered the proper colloid with which to combat this loss. Recent evidence indicates that whole blood is also needed in burn therapy. Whole blood is needed not only to prevent anemia, long observed to occur several days after burning, but also to replace the red blood cells that are destroyed after burning. Determination of hemoglobin and hematocrit levels gives no indication of this loss and cannot serve as a reliable guide for the volume of whole blood needed.

One of the most striking changes in burn therapy in recent years has been the more frequent acceptance of the open method of treatment. From the reports of several excellent investigators, it appears that the open method can be used with equally good results in some patients. The open treatment is not a treatment of neglect but a method which requires skill and a thorough knowledge of the principles of wound healing. This treatment must not be used for granulating surfaces. Some of its advocates do not advise its use for burns of the flexor surfaces of the neck, for circumferential lesions of the trunk, and for burns on the surfaces of joints of the legs and arms.

General agreement exists that full-thickness burns should be excised and the defect grafted as soon as this is feasible. Early excision and grafting shortens the period of protein loss from burned surfaces, diminishes infection and toxic absorption, and reduces scar formation. Immediate excision and grafting, however, may be prevented by the general condition of the patient, which may make additional trauma too hazardous, and the difficulty of immediately judging the depth of the burn. In burns of limited extent that are obviously full-thickness burns, early excision and grafting is the best treatment. In the patient with extensive burns, the additional trauma of anesthesia and operation may be contraindicated in the early stages of the burn. Excision of dead skin, however, once carried out, will improve the patient's condition at any stage. It is then a question of balancing these two factors with the fact that obvious full-thickness burns should be excised and grafted as soon as the patient can stand the operation. If the normal skin of the patient is insufficient for grafting or if the added trauma of taking a graft is felt to be unwarranted, homologous skin can be used to cover the wound as a temporary expedient. Because grafted skin is usually inferior to superficially burned skin that has regenerated, the ultimate result may be better if, in questionable cases, time is given for demarcation before skin is excised.

The early hope that corticotropin and cortisone might effect a permanent "take" of homologous skin has been shown to be ill-founded. In extensive burns, especially in children, the temporary covering of the open wound with homologous skin may be lifesaving, even though subsequent replacement with the patient's own skin is necessary.

Comment

It is hoped that in the future we can look forward to better ways of distinguishing superficial burns of first or second degree from deep burns of third degree. It is hoped, too, that we will achieve a better understanding of the "toxic" phase of a burn. Perhaps we shall find better débriding agents with a higher specificity for necrotic tissue, and, perhaps, better agents to stimulate epithelization. In spite of the development of many potent antibiotics, sepsis continues to plague the severely burned patient. All too frequently the patient survives burn shock, the toxic manifestation of the injury, and the early phases of treatment, finally dying from sepsis after several weeks. Local agents to control pain are no longer used. Gentleness in the care of the patient and early removal of necrotic skin, with early grafting, provide the best means of making the patient comfortable.

COMMITTEE ON REHABILITATION

The following report is the second in a series of articles which have been authorized for publication by the Committee. The first appeared in the Oct. 24 issue of THE JOURNAL, *page 1107. This series deals with various aspects of rehabilitation which are of interest to physicians.*
RALPH E. DE FOREST, M.D., *Secretary.*

TRAINING IN PHYSICAL MEDICINE AND REHABILITATION

Charles D. Shields, M.D.
and
Hugh H. Hussey, M.D., Washington, D.C.

Rehabilitation is a word that denotes restoration or improvement in condition. In medicine it is concerned with a type of practice which places broad social responsibilities on the physician. Physical medicine and rehabilitation is directed toward treatment of disability. It is concerned not only with medicine but with social, educational, and vocational opportunities for patients. The services of nurses, therapists, counselors, and teachers are utilized. The dedicated assistance of these coprofessional groups has done much to elevate standards of medical care. Individuals preparing themselves for medical practice today must be taught the methods and techniques of rehabilitation, along with their obligations and responsibilities to the numerous allied groups with whom they are associated in practice.

A New Medical Responsibility

The United States Army, in World War I, developed methods to shorten convalescence, provide vocational training, and return the soldier to work or to the highest level of self-care.[1] To accomplish this, a Division of Special Hospitals and Physical Reconstruction was formed in the Office of the Army Surgeon General in August, 1917. Excellent plans were developed for the care of the disabled. The Armistice of November, 1918, resulted in demobilization of trained medical personnel and in failure of this effort. During World War II, our present attitudes toward rehabilitation as a concept of medical practice were developed. The specialty of physical medicine and rehabilitation was organized to supervise and coordinate the work of various types of therapists and counselors in the care of neuromuscular diseases and certain musculoskeletal defects. This also provided diagnostic facilities, direct medical supervision, and continuous medical evaluation. Since the war, the scope of rehabilitation has developed and expanded, often under the leadership and insistence of lay groups. We must remember that the present status and usefulness of preventive medicine, public health, and psychiatry resulted from lay demands and not from any great foresight on the part of the medical profession. In the case of rehabilitation medicine, we must look beyond the immediate horizon and plan for the future, or once again we will suffer the embarrassment of doing the job after we have been pushed into position. Physicians as citizens have a great economic stake in the national rehabilitation program. During the history of our nation, when accident or disease resulted from military service and in more recent years from employment, full medical coverage has been regarded as the right of the patient. When he is not returned to a prior level of fitness, he is considered eligible for pension benefits. We cannot afford to have less than complete and superior rehabilitation services. These are, in the last analysis, a real economy. The techniques must be developed and improved by practice and research and properly taught to students in the health professions.

Teaching Rehabilitation to Medical Students

It is essential that a teacher understand for what he is preparing his students and that he have a plan or method to accomplish this goal. There is no "best method" or "only way." We believe that physical medicine and rehabilitation, under certain circumstances and in certain areas, should be practiced by competent specialists and, under all conditions, should be available to every physician engaged in any type of practice within the limits of his training, interest, and equipment. Physical medicine and rehabilitation is a medical specialty concerned with the management of patients who have disabilities that may benefit from physical diagnostic procedures, physical treatment, and broad rehabilitation services.

Georgetown University School of Medicine has recently developed a comprehensive rehabilitation program (see figure). Physical medicine and rehabilitation is taught in the second, third, and fourth years. Physical medicine is presented as a

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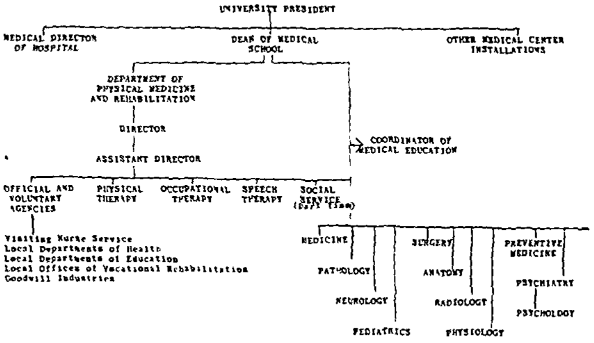
Professor and Chairman, Department of Physical Medicine and Rehabilitation (Dr. Shields) and Dean, Georgetown University School of Medicine (Dr. Hussey).

special field of practice concerned with the diagnosis and treatment of neuromuscular diseases and certain musculoskeletal defects. Rehabilitation is presented as a complex responsibility that affects all departments in the medical school.

The department of physical medicine and rehabilitation has the status of a major department and directs and coordinates the total program. It is represented on the executive faculty by the chairman of the department. It is concerned with the presentation of material to students that will acquaint them with the specialty and with the obligations of the physician to obtain, for certain of his patients, services that are beyond the confines of individual medical practice. The student is impressed in this manner with his obligation to assume responsibility for return of his patient to the vocation of his choice or to the highest level of self-care consistent with the residuals of his illness or injury. Case presentations, seminars, and conferences are the usual techniques of teaching the subject. These are frequently interdepartmental, with members of coprofessional groups participating. In this manner, integrated and coordinated medical care is demonstrated, as well as the relationship of nurses, therapists, and counselors to the physician. The student is introduced not only to his medical responsibilities in this area but also to his direct advisory functions to the social, educational, and vocational services essential to the welfare of the patient.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PHYSIOLOGY
PREVENTIVE MEDICINE
PSYCHIATRY
PSYCHOLOGY

Organizational plan for teaching physical medicine and rehabilitation, Georgetown University School of Medicine, Washington, D. C.

Techniques and methods must be demonstrated as well as discussed with students. Departments of physical medicine and rehabilitation must, therefore, be developed to a reasonable standard of excellence to provide the means for this accomplishment. This is an expensive effort, and personnel are not always readily obtainable. Medical leadership is necessary to furnish diagnostic and evaluation services along with direct supervision of coprofessional groups. In our department of physical medicine and rehabilitation, physical therapy, occupational therapy, and speech therapy are established as sections. A prevocational testing laboratory emphasizes clerical skills. Social service is available on a part-time basis. Psychological services are obtained through the department of psychiatry. There are direct and pleasant relationships with all other school and hospital departments and with outside official and voluntary agencies.

The department of physical medicine and rehabilitation was established at Georgetown University in 1954. At this time, the department was assigned responsibility for eight lectures to the junior class and for training senior clerks who were assigned to the University Hospital service. This effort was a resounding failure because a department must be well established before it can serve in an effective manner for teaching purposes. Physicians properly trained in the specialty are scarce. When one or two are available and are engaged in a busy hospital practice establishing and operating a service, they have little time to associate themselves with the clerkship method of instruction. After consideration of the problem, it was decided to join the older and well-established departments, to utilize their conferences, seminars, and, on occasion, ward rounds, in order to present the fundamentals of rehabilitation medicine. These difficulties may have stimulated a new method of teaching now in use at our school, characterized by fewer lectures and increased number of interdepartmental conferences.

The cost of instruction in physical medicine and rehabilitation at Georgetown University is augmented by a training grant from the Office of Vocational Rehabilitation. The teaching program is as follows:

Second Year.—During the second year the department of physical medicine and rehabilitation takes part in teaching activities as follows:

Preventive Medicine: In the teaching of preventive medicine, the idea of directing the activities of coprofessional groups is developed. For example, a social worker presents a request received from the physician and then discusses the results of her interview and evaluation; a physical or occupational therapist reads the prescription of the physician and demonstrates by use of a patient the methods by which she approaches the goal of therapy.

Physical Diagnosis: In the teaching of physical diagnosis, material is presented concerning the evaluation of weakness and methods of grading and recording muscle weakness, fascial tightness, and measurement of joint range of motion.

Conferences on Mechanisms of Disease: During the second semester of the sophomore year, 68 conferences on the mechanisms of disease are conducted. The department of physical medicine and rehabilitation takes part in certain of these conferences. Two of these are musculoskeletal trauma, in which general surgery and orthopedic surgery are the other participants, and disorders of muscle, in which the departments of pathology and neurology participate.

Third Year.—During the third year there are 128 conferences on diagnosis and treatment, each lasting two hours. The department of physical medicine and rehabilitation is represented in 16 of these interdepartmental activities. Because the emphasis here is on diagnosis and treatment, methods of using therapist and counselor services are frequently presented, in addition to methods and indications for therapy.

Fourth Year.—During the fourth year the department of physical medicine and rehabilitation shares teaching beds with the department of neurology. Senior clerks are assigned to this service. On one day each week, a member of the department of physical medicine and rehabilitation conducts the rounds and emphasizes therapy and rehabilitation rather than diagnosis. This method is of mutual advantage to the departments of neurology and physical medicine and rehabilitation. Members of the department of physical medicine and rehabilitation take part in ward rounds conducted by other departments on request. It is our experience that this teaching schedule taxes the capacity of two full-time teachers who also operate the department of physical medicine and rehabilitation in the University Hospital.

Training Residents in Physical Medicine and Rehabilitation

Physical medicine and rehabilitation is a broad specialty that offers varied fields of interests to the resident and one which requires much cooperation from many departments in the medical school and hospital. A minimum of three years of residency training is considered necessary to train a physician who desires to specialize in this field. During this period, instruction at the graduate level in anatomy, physics, biophysics, and pathology is essential. Special courses in these sciences are arranged as follows:

1st Year of Residency:
Anatomy
  Neuroanatomy—4 semester hours, lectures 2 hours per week, laboratory 4 hours per week (one semester).
  Anatomy—Musculoskeletal system, 2 semester hours arranged with the department of anatomy in regular courses of instruction in the medical school.
Physiology
  Neuromuscular Physiology—2 semester hours.
  Physiology of Respiration—2 semester hours. These courses are arranged with the department of physiology in the medical school.
2nd Year of Residency:
  Physics—2 semester hours.
  Biophysics—2 semester hours. Presented by personnel in the department of physical medicine and rehabilitation.
All Years of Residency:
  Pathology—Residents attend all death conferences.

Clinical aspects of training are presented in the usual graded manner, with gradually increasing responsibility for patient care. It is therefore essential that teaching beds be provided for this purpose. At Georgetown University Hospital, 20 beds are shared with the department of neurology. Again, in teaching residents, there is a close relationship between these two departments.

Residents are obliged to attend all conferences and ward rounds of the departments of physical medicine and rehabilitation and neurology as well as medical and surgical grand rounds. Residents in physical medicine and rehabilitation are assigned for specific training purposes for short periods to the departments of medicine, neurology, surgery, anesthesiology, psychiatry, and physiology. During these assignments, they are under the direct supervision of the department of physical medicine and rehabilitation and are absent only for specific training purposes and not for routine assignment. This is to provide continuous, concentrated; and supervised training in the special field of physical medicine and rehabilitation and to prevent mere utilization of residents' services by other departments.

Arrangements are made for the second-year and third-year residents to assume increasing responsibility for outpatients and to spend time in voluntary and official agencies under proper medical and other appropriate supervision to observe social, educational, and vocational services for the disabled. It is our opinion that adequate practice facilities must be provided by affiliation. The resident is assigned for certain periods of time to a psychiatric rehabilitation service, a tuberculosis rehabilitation service, an official vocational rehabilitation agency, a cerebral palsy center with complete services, and an educational program with rehabilitation services.

We are firm in our opinion that physical medicine and rehabilitation cannot be taught to residents isolated from other special interests in medicine. It must be a major activity within the hospital. Residents in physical medicine and rehabilitation are taught important fundamentals in other medical specialties. This insures that residents in other specialties will develop knowledge concerning physical medicine and rehabilitation and will learn to use and respect it accordingly. The resident in physical medicine and rehabilitation thus develops the broad foundation upon which success of his training depends. He will, at the same time, learn his own limitations and those of his special field in medicine.

Summary and Conclusions

Medical school curriculums should include provision for instruction in the field of physical medicine and rehabilitation. A method of teaching this subject to medical students considers availability of limited numbers of trained teachers, utilizes existing facilities of other departments in the school, and creates a high level of mutual understanding among members of the faculty. Development and expansion of the specialty of physical medicine and rehabilitation demand that young physicians become interested and trained in the specialty. Instruction of residents in this area of medicine provides broad training in a field of wide responsibility and considers economy of personnel, space, and equipment.

Reference

1. United States History of World War, Medical Department of United States Army in World War, vol. 13, 1927.

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TRAINING FOR TOMORROW

IN NO area of medical instruction is there a greater need for long-range vision than in the department of internal medicine in a teaching hospital allied with a medical school. Such a department, responsible for medical training in its broadest sense, may be expected to define and to implement the pattern of conduct for other departments to follow in the clinical sciences. One may inquire justifiably, why it is necessary to establish a pattern of conduct for the future when our medical schools and teaching hospitals are credited with performing a thoroughly commendable job at the present time. It is not necessary to search deeply to discover the answer. Although the obvious is not appreciated widely, and hence lacks the general recognition that it deserves, the absorption and comprehension of medical knowledge available today by young physicians in training does not automatically insure continued ability to absorb and to comprehend the medical knowledge that will become available tomorrow. Equal in importance to the task of communication of the latest and best of today's information must be the keen awareness of what is not yet discovered and that, when it is revealed at some future time, the physician in practice will be prepared to digest and to assimilate the new. Only with such a philosophy will the patient continue to be the recipient of the best medical care.

The responsibility for the direction of training today and the planning for tomorrow resides largely in the faculties of our medical schools. To be sure, medical associations, research foundations, and the National Institutes of Health contribute immeasurably: agencies and institutions which should work hand in hand with the teachers and officers of the medical schools. The volume of clinical problems, the magnitude of investigations in progress, and the size of the professional groups places the department of internal medicine in a foremost position in the medical faculty. Thus the pattern of conduct for such a department becomes crucial. Dr. Walter Bauer, Jackson Professor of Medicine at Harvard Medical School, has presented a clear narrative of the program at the Massachusetts General Hospital for the training of medical students, interns, research fellows, training fellows, and graduate students in the broad field of internal medicine. A description of the fundamental precepts of the training program was presented in the Presidential Address at the annual meeting of the Association of American Physicians in Atlantic City, May 5, 1959. The address appears in this issue of The Journal (page 1277).

The address is an exposition of a highly imaginative and effectively coordinated protocol of group responsibility. Concentration within the field of internal medicine is considered vital. Basic scientists actively participating in the training of physicians in clinical departments as well as advancing the frontiers of knowledge by means of isotopes, electrophoretic patterns, and exploration of enzyme systems are integral components of the group. Qualified volunteer physicians have an equally vital assignment within the corporate structure. A pattern of conduct such as that in effect at the Massachusetts General Hospital is not the only instrument to insure a successful goal. Other medical faculties are exploring diverse ways and means to accomplish similar objectives. The MGH plan is deemed worthy of examination, however, in order that the primary purpose of the teaching hospital, i. e., the care of the sick, be fulfilled. This is best achieved by advancing knowledge through research in their own laboratories, utilizing knowledge disseminated from other laboratories, and finally by accepting the concept that contemporary medical training must be imaginative as well as profound in order that the physician in training today will continue to provide the best care and service to the person who becomes a patient tomorrow.

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COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

On recommendation of the Residency Review Committee for Obstetrics and Gynecology, its three sponsoring organizations, the American Board of Obstetrics and Gynecology, the American College of Surgeons, and the Council on Medical Education and Hospitals of the American Medical Association have adopted the following principles of residency approval in this specialty. Recommendations one through nine deal with matters of procedure within the Committee; recommendations 10 through 13 represent changes in policy which are in accordance with the "full training" concept of graduate education. The attention of physicians participating in residency programs in this specialty is called to the fact that after July 1, 1962, residency programs not including, either intramurally or through affiliation, 36 months of clinical training in obstetrics and gynecology, will no longer be approved.

WALTER S. WIGGINS, M.D., *Secretary.*

RESIDENCY TRAINING IN OBSTETRICS AND GYNECOLOGY

1. Reports of the field staff on residency programs are distributed by the Secretary to Committee members for review prior to each meeting; these reports are then considered by the Committee as a whole at the next meeting and appropriate action taken. An *ad hoc* committee may be appointed to act for the Committee in such instances as are designated.

2. After reviewing a program, the Committee may approve, provisionally approve, disapprove, defer action, or place program on probation. In the event of an action other than approval, specific reasons for such action are to be stated in the letter of notification.

3. When approval is granted, this approval is considered retroactive to the beginning of the current year of service for any resident on duty, or to the date of application for approval, whichever date is earlier.

4. When a training program does not meet the requirements for continuation of approval, but has the potential for doing so, that program may be placed on probation until requirements are met. A period of 12 to 18 months is allowed for correction of deficiencies. If correction has not been accomplished by the specified date, appropriate action will be taken.

5. When a training program is not yet in full operation but shows promise of meeting all educational requirements, the program may be granted provisional approval, subject to early review.

6. When a previously approved training program cannot meet requirements, the effective date of withdrawal of approval, after fair warning, shall be determined by the Committee.

7. Routine surveys of residency training programs will be made at periodic intervals by the field staff of the Council.

8. The Committee can, at any time, request reinspection of a program by either a member of the Council field staff or a regional evaluator representing the Committee. The Council shall be responsible only for expenses incurred by its field staff in making such inspection. The expenses incurred by the regional evaluators shall be borne by the other sponsoring organizations.

9. Listing of approved programs in the Internship and Residency Number of THE JOURNAL of the American Medical Association shall be the responsibility of the Council, and listing in the *Bulletin of the American College of Surgeons* shall be the responsibility of its Board of Regents.

10. Beginning July 1, 1962, one-year programs approved only for the first year in obstetrics and/or gynecology will not be approved and the institutions involved are urged to affiliate with programs offering full training. In the programs offering affiliation, approval will be given only to the parent program.

11. Two-year residency programs in obstetrics and gynecology will not be approved after July 1, 1962. Institutions offering two-year programs are encouraged to expand to three years or affiliate with a full program.

12. Two-year residencies in gynecology only and in obstetrics only will not be approved after July 1, 1962. They should affiliate to produce a program which can be approved.

13. While training in general surgery, internal medicine, and urology is desirable, such training should not be a part of the three years' required clinical program in obstetrics and gynecology. A minimum of 18 months in obstetrics and 18 months in gynecology is required. Likewise, formal courses in the basic sciences which separate the resident from clinical training should not be included in the three-year minimal clinical training program.

COUNCIL ON NATIONAL DEFENSE

COURSES ON MANAGEMENT OF MASS CASUALTIES

The following dates for civilian physicians to attend Management of Mass Casualties courses at Army Medical Service School, Brooke Army Medical Center, Fort Sam Houston, San Antonio, Texas, are still open: Nov. 30-Dec. 4, 1959; Feb. 15-19, 1960; April 25-29, 1960; and June 13-17, 1960. There are spaces for two civilian physicians for each of these scheduled courses, except that of Feb. 15-19, 1960, for which one space is still open. These quotas are made available to the A. M. A. Council on National Defense by the Office of the Surgeon General, Department of the Army. Physicians interested in attending are requested to write directly to the Council on National Defense.

PUPIL SAFETY IN DISASTER

With the cooperation of the Office of Civil and Defense Mobilization, the American Association of School Administrators has published a pamphlet for school administrators who are developing school disaster protection programs. Entitled "Disaster Protection Handbook for School Administrators," the emphasis is on pupil safety under disaster conditions. Copies may be obtained from OCDM.

GOVERNMENT SERVICES

NAVY

Defense Course.—A four-weeks' course in ABC (atomic, biological, and chemical) warfare defense, for active duty medical department officers possessing security clearance, will convene at the U. S. Naval Schools Command, Treasure Island, San Francisco, Calif., on Jan. 4, 1960. A class quota of 50 has been assigned. Ten spaces will be reserved for Army and Air Force officers. The breakdown for the Navy will be 30 Medical Corps, 5 Dental Corps, and 5 Medical Service Corps officers.

During the course the medical aspects of modern warfare and of military peacetime operations including problems incident to atomic, biological, and chemical weapons systems, nuclear propulsion, mass casualties, and isotope programs will be stressed. Military aspects of the weapons systems and military countermeasures will also be considered so that medical officers may function effectively on a staff and can reasonably assess the medical compromises imposed by the military situation. Outstanding speakers, both military and civilian, will be featured on the program. Visits will be made to the Navy Radiological Defense Laboratory and the Naval Biological Laboratory, as well as practical exercises and drills. All students will be supplied textbooks on a permanent retention basis.

Eligibility for Navy officers is as follows. 1. Requests for attendance are invited from medical officers; reserve officers of the Medical Corps whose attendance would obviously assist them in the performance of their duties will be considered providing they have a minimum of 20 months of obligated service remaining. 2. The dental officers to attend will be selected by the bureau of medicine and surgery. 3. Requests are invited from senior Medical Service Corps officers. Priority will be given to officers assigned duties on fleet and/or district staffs, and administrative officers of Naval hospitals. Interested officers with the foregoing requirements must submit a written request via their commanding officers, to reach the bureau of medicine and surgery (Attn: code 316), prior to Nov. 15, 1959.

Personal.—Capt. Paul R. Engle recently reported to the bureau of medicine and surgery for duty as deputy director, physical qualifications and medical records division.——Rear Adm. J. L. Holland, M. C., assumed command of the Naval Aviation Medical Center, Pensacola, Fla., in September. He is the first flag officer of the Navy Medical Corps ever to serve on active duty in Pensacola.

VETERANS ADMINISTRATION

Computer for Cardiac Diagnosis.—An electronic data computer for the study of heart disease was developed by a Veterans Administration–National Bureau of Standards research team consisting of Leonard Taback, Ethel Marden, H. L. Mason, Dr. Hubert V. Pipberger, and Dr. Edward D. Freis. Electrical impulses from the heart are recorded, converted to a numerical system, and fed into an electronic computer, which is set up to provide the physician with quantitative data on major characteristics of the heart. The device appears to promise more complete information than has been available from the electrocardiogram and also to be economically feasible for wide use.

Award to Dr. Lyon.—The Veterans Administration has given its highest award, the Exceptional Service award, to Dr. George M. Lyon, for his pioneering work in atomic medicine. In presenting the award the administrator of Veteran Affairs, Sumner G. Whittier, said:

"Recognizing the tremendous potential of atomic force for good and harm, Dr. Lyon became an active participant in the study of its biologic and medical applications. Under his energetic guidance, the Veterans Administration became a leader in the application of radioisotopes to research, diagnosis, and treatment. Its record of safety in this virgin field has been a model for similar enterprises. The monitors trained under this program will be an invaluable asset in the event of nuclear attack or accident."

Medical Advisory Group.—Five new members have accepted appointment to the Veterans Administration special medical advisory group. The group meets quarterly to advise the Administrator of Veterans Affairs and the VA Chief Medical Director on the VA medical program. The new members, four of whom are replacements for former members whose terms have expired, are (1) Dr. Jasper L. Callaway, professor of dermatology and syphilology at Duke University, who replaces Dr. Clarence S. Livingood, chief of the dermatology department of Henry Ford Hospital in Detroit; (2) Dr. Arthur G. DeVoe, professor and chairman of the department of ophthalmology of New York University Post-Graduate Medical School and director of eye service at Columbia University Hospital, who replaces Dr. Harold G. Scheie, professor of ophthalmology at the University of Pennsylvania; (3) Dr. Raymond J. Nagle, dean of the College of Dentistry of New York University, who replaces Dr. Clemens V. Rault, dean of Georgetown University School of Dentistry; (4) Dr. Ralph M. Tovell, director of the department of anesthesiology of the Hartford (Conn.) Hospital, who replaces Dr. Donald E. Hale, head of the anesthesiology department of the Cleveland (Ohio) Clinic Hospital; and (5) Dr. O. Currier McEwen, associate professor of medicine at New York University and formerly chief consultant in medicine in the European theater of operations during World War II, who replaces Dr. Richard P. Stetson, who resigned from the special medical advisory group to become area director of professional services in the Boston VA area medical office.

Personal.—Dr. Martin M. Cummings, director of medical research for the Veterans Administration in Washington, D. C., left the VA in October to become chairman of the department of microbiology at the University of Oklahoma School of Medicine in Oklahoma City. He will continue to be affiliated with the VA as a consultant to the agency's Oklahoma City Hospital, where he also will do research on sarcoidosis.

U. S. Contributes to Malaria Eradication.—Dr. Leroy E. Burney announced that the United States will contribute 2 million dollars to the Pan American Health Organization's malaria eradication campaign in 1960. This makes the United States total contribution to this PAHO fund $8,500,000 since 1956. The United States will also make a contribution of 3 million dollars to the Special Malaria Eradication Account of the World Health Organization.

PUBLIC HEALTH SERVICE

Limitation of Activity.—Chronic conditions affecting health limit the normal activity of an estimated 17 million people in the United States, according to findings developed from nationwide household interviews conducted by the Public Health Service. The information recorded about individual persons is confidential, and only statistical totals are published. These 17 million persons, representing 10% of the population, are limited in their ability to work, keep house, or pursue outside activities. A segment of this group amounting to 3% of the population or an estimated 4,855,000 persons have trouble moving about or cannot move about without help. Of the latter group, about 1 million persons are completely confined to their homes. The figures do not include military personnel or people in mental or other types of long-term institutions.

Activity limitations were reported most frequently among low income families and older people. Among families with incomes of less than $2,000 a year, 20% had some activity-limiting condition; for those with incomes of $7,000 or more, only about 7% were similarly limited. About 1.4% of the children under 15 years of age have some activity limitation, whereas about 50% of the persons 75 years of age and older fell in this category. The report is entitled "Limitation of Activity and Mobility Due to Chronic Conditions, United States, July 1957-June 1958," Public Health Service Publication no. 584-B 11. Copies may be obtained from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 30 cents each.

Study on the Stein-Leventhal Syndrome.—An investigation of the role of the adrenal gland in the Stein-Leventhal syndrome has been initiated at the Clinical Center, National Institutes of Health. Salient features in this syndrome include oligomenorrhea, hirsutism, and polycystic ovaries. The cooperation of interested physicians in referring laparotomy-proved cases is invited. Referral letters will receive prompt attention and should include detailed medical information about the patient. Accepted patients will be studied for varying periods up to several weeks. On completion of their study, patients will be returned to the care of their referring physician, who will also receive a detailed report. In some instances it may be desirable to arrange for occasional follow-up visits to the clinical center. These would supplement rather than substitute for visits to the patient's own physician.

Physicians interested in the possibility of referring patients should write to (1) J. E. Rall, M.D., chief, clinical endocrinology branch, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Md., or (2) Saul W. Rosen, M.D., clinical associate, National Institute of Arthritis and Metabolic Diseases, Bethesda 14, Md.

Personal.—Dr. Donald Roger Chadwick of the Public Health Service was appointed as secretary of the Federal Radiation Council.——Dr. Robert W. Wilkins, of Boston, was appointed to the National Advisory Heart Council for a four-year term. He is one of the world's foremost authorities on hypertension.——Dr. Joseph A. Gallagher was appointed to the headquarters staff of the division of Indian Health of the U. S. Public Health Service in Washington, D. C. He moves to Indian health headquarters as a member of the staff in hospital administration after three years as medical officer in charge of the division's Alaska Native Health Service Area office at Anchorage.

NATIONAL SCIENCE FOUNDATION

Graduate Awards.—Applications are being accepted for National Science Foundation Graduate Fellowship awards for advanced study in the sciences, including medicine. Fellows will be selected on the basis of ability as attested by letters of recommendation, academic records, and other evidences of attainment. Applicants must take the graduate record examination. Applicants' qualifications will be evaluated by carefully chosen panels operating under the aegis of the National Academy of Sciences—National Research Council. Stipends for these fellowships vary with the academic status of the fellows. First-year fellows (students entering graduate school for the first time or those who have had less than one year of graduate study) will receive annual stipends of $1,800. Fellows who need one final calendar year of training for the doctoral degree will receive annual stipends of $2,200. Fellows between these two groups will receive stipends at the rate of $2,000 annually. A dependency allowance of $500 per annum for spouse and for each dependent child will normally be available to married fellows. Tuition, laboratory fees, and limited travel allowances will also be provided.

Application material for the graduate fellowship program may be obtained from the Fellowship Office, National Academy of Sciences—National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C. The closing date for the receipt of applications is Jan. 1, 1960. Final selection of fellows will be announced March 15, 1960.

FOOD AND DRUG ADMINISTRATION

Bust Developers.—Mechanical contrivances for increasing the size of women's breasts are a swindle and a potential hazard to health and are considered illegal per se. The Food and Drug Administration seized one make of these devices at Tampa and Clearwater, Fla., and Phoenix, Ariz. The seized devices, involving an electric air pump and plastic suction cups, were alleged to be dangerous to health and to be misbranded by false and misleading labels claiming to increase the size and firmness of the breasts.

Colored Light Not a Cancer Cure.—Exposing the body to colored light will not cure cancer or any other serious disease. The Food and Drug Administration seized component parts for color lamps promoted with cure-all health claims. The promoter sold the device in do-it-yourself assembling kits, consisting of a lamp base, electrical fixtures and wiring, and plastic slides in a set of five colors. The promoter, in his literature, offered the device as a cure for leukemia, tumors, glaucoma, arthritis, rheumatism, bursitis, neuritis, anemia, asthma, tuberculosis, all diseases of the eye, nose, and throat, measles, whooping cough, scarlet fever, influenza, and all diseases which may affect the body of man.

Voluntary Actions by Food and Drug Firms.—Improvements costing nearly 4 million dollars were made voluntarily by food and drug manufacturers and warehousemen in the fiscal year 1959 to aid in protecting consumers. In addition, 8,000 tons of unfit foods and $176,000 worth of substandard drugs were removed from the market in 1,228 voluntary actions. This report covers only those actions observed by or reported to Food and Drug Administration inspectors. Many similar actions were undoubtedly taken by other firms and did not come to official notice. Voluntary corrections included improvements of plant sanitary conditions, improvement of processing and storage practices, and disposal of unfit products.

MEDICAL NEWS

ALABAMA

Heart Center Dedicated.—Dedication of the University of Alabama Medical Center's cardiovascular unit to the memory of the late Dr. Luther Leonidas Hill Jr., pioneer Alabama surgeon, was held Oct. 18. Events included the dedication ceremony, a reception for invited guests, and a tour of the Luther Leonidas Hill Heart Center. Among those participating were Sen. Lister Hill, son of Dr. Hill and senior U. S. Senator from Alabama. Dr. Luther L. Terry, senior investigator and assistant director of the National Heart Institute, Bethesda, Md., was the featured speaker. A namesake of the late Dr. Hill, Dr. Terry is from Red Level. Dr. Luther Leonidas Hill, who practiced in Montgomery for nearly half a century, was the first physician in America to report a successful suture of the human heart. He performed this operation in 1902 on a 13-year-old boy who had received a stab wound penetrating the left ventricular cavity. Dr. Hill was elected president of the Medical Association of Alabama in 1897.

CALIFORNIA

Dr. Geiger Honored.—At a banquet Sept. 5 the "Distinguished Service" silver scroll with bronze coat of arms medallion of the Pan American Medical Association was presented to Dr. Jacob C. Geiger, San Francisco.

COLORADO

Scholarship to Aid Medical Students.—The Denver Medical Society announced the establishment of a $100,000 scholarship fund to aid "gifted and deserving medical students" at the University of Colorado School of Medicine, Denver. Dr. Carl A. McLauthlin, chairman of the society's board of trust, said the fund was made possible by the gift of $100,000 from Miss Grace Isabelle McNaught in memory of her father, Dr. Francis H. McNaught, after whom the fund will be named. Dr. McNaught was a professor of operative obstetrics in the University of Colorado School of Medicine and was the only Colorado doctor ever to serve as president of the Colorado State Medical Society for two years. The fund will be administered by the trustees of the medical society.

CONNECTICUT

Lecture on Schizophrenia.—The Yale Medical Society will present "Current Biochemical Theories of Schizophrenia" by Dr. Seymour S. Kety, chief, Laboratory of Clinical Science, National Institute of Mental Health, Bethesda, Md., on Tuesday, Nov. 10, 5 p. m., in Fitkin Amphitheater, at the Yale–New Haven Medical Center, New Haven. Physicians on call should leave the number LOcust 2-1161, Ext. 865.

GEORGIA

Conference on Nutrition.—The second "Better Foods for Better Nutrition Conference," a joint conference sponsored by the divisions of foods and nutrition and food processing of the University of Georgia, will be held March 3-4, 1960, at the Center for Continuing Education, University of Georgia, Athens. This conference is planned for persons engaged in research, extension, and teaching of foods and nutrition or food technology, as well as home economists in business, lunchroom supervisors, hospital dieticians, public health nutritionists, and handlers and processors of foods. Special attention will be given to industrial and institutional problems in processing, handling, and serving foods. For information, write John J. Powers, Ph.D., Head, Department of Food Technology, College of Agriculture, University of Georgia, Athens.

ILLINOIS

Hospital News.—On Sept. 3, Dr. T. B. McMurry, of the University of Capetown, South Africa, addressed the weekly staff conference in orthopedic surgery at Hines Veterans Administration Hospital. His subject was "Recurrent Dislocation of the Shoulder."——Forest Hospital, Des Plaines, appointed Dr. Kalman Gyarfas, Chicago, as consultant of the psychiatric training program. Dr. Gyarfas will help to plan and implement a training program for nonpsychiatric interns and residents in the community. He will also serve as consultant on the hospital's other educational programs and for its research programs.

Chicago

Dr. Visotsky Named Mental Health Director.—Dr. Harold M. Visotsky, assistant professor of psychiatry, University of Illinois College of Medicine, was appointed director of mental health for the City of Chicago. He will head the program of the mental health section of the Chicago Board of

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Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

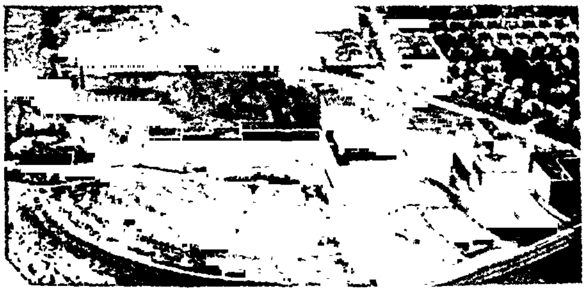
Health under Dr. Herman N. Bundesen, president. His appointment became effective Sept. 1. Dr. Visotsky succeeds Dr. Henry Fineberg, formerly head of the psychiatric department at Children's Memorial Hospital, who in January, 1958, consented to serve as acting director of the mental health unit until a full-time director was named.

Dr. Strauss Honored.—Dr. Sidney Strauss was honored by the Chicago Heart Association, which he helped found in 1922, at an open house celebration held at the association's new headquarters at 22 W. Madison on Sept. 24. Dr. Strauss, 81, is senior attending physician at the Michael Reese Hospital whose staff he joined in 1911. Dr. Strauss was among a small group of physicians who established what was originally called the Association for the Prevention and Relief of Heart Disease, later changed to the Chicago Heart Association in 1925. In 1924 he helped organize the American Heart Association and was a member of the first board of directors. The Sidney Strauss Conference Room was dedicated to him at the new headquarters Sept. 24.

Professor Knaus to Lecture.—Prof. Hermann H. Knaus, director, department of gynecology and obstetrics, Hospital of Vienna-Lainz, Austria, will present a lecture, "Post-Maturity, Determination and Treatment," Nov. 19, 4:30 p. m., in Dora DeLee Hall, The Chicago Lying-in Hospital, of the University of Chicago School of Medicine.

MARYLAND

New General Hospital in Baltimore.—The new Sinai Hospital, reportedly the only general hospital in the northwest section of Baltimore, was dedicated Sept. 20 and will be officially opened in November. The hospital, built at a cost of over 20 million dollars, has a total of 483 beds, 171 more than there are at the old Sinai on Monument Street. It is composed of nine units, including the Mount Pleasant Building completed in 1953, covers 600,991 square feet of space, has parking facilities for over 800 cars, a heliport, and overnight accommodations for relatives for very ill patients. Besides the Mount Pleasant Building, other units are the General Hospital Building, Louis and Henrietta Blaustein Obstetric and Gynecology Building, Morris Schapiro and Family Research Building, Hecht School of Nursing, Hoffberger Nurses Residence, Rosenbloom Staff Residence, Zamoiski Auditorium, and Bettie S. Fuechsl and Ferdinand and Henrietta Fuechsl Service and Utility Buildings, all connected by underground corridors. Except in the pediatric department, there are no more than two beds in any room, even in the wards. Patient rooms are provided with individual control for air-conditioning, have piped-in oxygen and suction, and private lavatories. There are 40 beds to each nursing station, and each 40-bed unit has its own solarium. For very ill patients there will be two intensive nursing units of four beds each. Ten operating rooms radiate from a central sterile and scrub-up area. The buildings have been so constructed that additional floors and wings can be added. There are 40 acres of land available for future expansion. The Aaron and Lillie Straus Out-Patient Department can handle 100,000 patient visits a year, and the Kann Memorial Emergency Service is equipped to handle several hundred patients a day. The new hospital is located on 50 acres of land. It is contemporary in design, built of red brick with white Vermont marble used for outside trim and Israeli marble used in the lobby of the General Hospital Building. The hospital, a constituent agency of the Associated Jewish Charities, is nonsectarian.


The new Sinai Hospital, Baltimore.

MASSACHUSETTS

Dr. Gross Receives Heart Award.—The 1959 Albert Lasker Award of the American Heart Association was presented Oct. 24 to Dr. Robert E. Gross, Boston. The award, given annually "for distinguished achievement in the field of cardiovascular research," was conferred during the association's annual scientific sessions. Dr. Gross, the first surgeon to be thus honored, is Ladd Professor of Children's Surgery at Harvard Medical School and surgeon-in-chief at Boston's Children's Hospital. He is a founder and a member of the board of directors and executive committee of the American Heart Association. The Lasker award for cardiovascular research was established in 1953 by the Albert and Mary Lasker Foundation in cooperation with the American Heart Association. Previous winners include Dr. Paul Dudley White, Boston; Dr. Albert Szent-Gyorgyi, Woods Hole, Mass.; Dr. Carl J. Wiggers, Cleveland Heights, Ohio; Dr. Louis N. Katz, Chicago; Dr. Isaac Starr, Philadelphia; and Dr. Irvine H. Page, Cleveland.

MICHIGAN

Dr. Gray Honored.—Dr. Jacques Pierce Gray, Detroit, visiting lecturer of the American Medical Writers' Association, was recipient of the Distinguished Service Award of the association for 1959. The award is given annually to a fellow of the association "who has made distinguished contributions to medical literature or rendered unusual and distinguished services to the medical profession."

Dr. Walker to Give Annual Lecture.—Dr. A. Earl Walker, Baltimore, professor of neurosurgery and chairman of the department of neurological surgery at Johns Hopkins Hospital, will present the annual Alpha Omega Alpha Lecture at Wayne State University College of Medicine, Detroit, Nov. 20, 11 a. m. to 12 noon in the Wayne County Medical Society Auditorium. The subject he has chosen is titled "A Modern View of the Falling Sickness."

Emeritus Professors Receive Honorary Degrees.—Honorary doctor of law degrees were presented at the annual University of Michigan Medical Honors Convocation Oct. 17 to Drs. Frederick A. Coller and Udo J. Wile, emeritus professors of the University of Michigan Medical School, Ann Arbor. The convocation closed the three-day meeting of the seventh Triennial Medical Alumni Conference. Dr. Coller, major speaker at the convocation, retired in 1957 after serving as head of the surgery department for 27 years. The Frederick A. Coller Society, founded in 1947, is made up of surgeons who trained under him. He is one of 50 members of the Royal College of Surgeons in England. Dr. Wile, professor emeritus of dermatology and syphilology and chairman of the department for 35 years, was cited for his "contributions to the scientific knowledge of diseases and his advances in medical theory and practice." Dr. Wile reportedly established the first university hospital clinic in the United States for training dermatologists and syphilologists.

MINNESOTA

British Lecturer.—Dr. James Purdon Martin, emeritus chief of staff in the National Hospital for Neurologic Diseases and Epilepsy, Queen's Square, London, England, gave a lecture, "Extrapyramidal Dyskinesias," at the Mayo Foundation, Rochester, Sept. 29.

Dr. Buie Named Royal Society Member.—Dr. Louis A. Buie Sr., Rochester, founder of the section of proctology of the Mayo Clinic and a member of the staff from 1919 until his retirement in 1955, was made an honorary member of the Royal Society of Medicine of England on July 1. The certificate of honorary members, signed by Dr. Henry R. Thompson, London, president of the society, indicates that the honor was conferred on Dr. Buie "for distinguished services to science."

MISSOURI

Foreign Lecturer.—Dr. S. C. Sen, radiologist of New Delhi, India, lectured Oct. 9 in the University of Missouri Medical Center Auditorium. His subject was "Brief Glimpses into Ancient Indian Medicine and Traditional Chinese Medicine." Since 1947 Dr. Sen has been a member of the Council of the World Medical Association and was its secretary for Asia for nine years.

NEW YORK

Dr. Yanover Cited.—On Sept. 3 Dr. Robert R. Yanover, Flushing, chairman of the medical advisory board of Abilities Inc., Albertson, was given a presidential citation, "for his contribution to the advancement of the disabled." Abilities Inc., with which Dr. Yanover has been associated since its founding seven years ago, is an electronics manufacturing firm employing only disabled persons.

Alumni Honor Dr. McCann.—Dr. William S. McCann, Rochester, was presented the annual Gold Medal Award at the 15th annual meeting of the University of Rochester Medical Alumni Association, Oct. 10. Dr. McCann, who retired on June 30, 1957, as chairman of the department of medicine, a position he had held since the School of Medicine and Dentistry was opened in 1925, is now emeritus professor of medicine.

Radio Medical Conferences.—Albany Medical College inaugurated its fifth season of two-way radio medical conferences Oct. 6, Dr. Frank M. Woolsey Jr., Albany, associate dean and director of postgraduate education, announced. The conferences are broadcast to doctors at 24 hospitals in New York, Massachusetts, and New Hampshire. The current season will extend through April, 1960, with conferences scheduled on a three-times-a-week basis. The hour-long conferences cover a variety of medical and surgical topics. Last year, more than 700 individual physicians took part in one or more conferences. The total attendance for the year was 5,425. Albany Medical College broadcasted its initial conference in December, 1955. E. R. Squibb & Sons, pharmaceutical division of the Olin Mathieson Chemical Corporation helps support the conferences by a grant-in-aid. Faculty members from six eastern medical schools participate.

New York City

Biologist to Give Annual Lecture.—The fifth annual Israel S. Wechsler Lecture will be given Dec. 11, 8:30 p. m., in the Blumenthal Auditorium of the Mount Sinai Hospital. Paul A. Weiss, Ph.D., head, department of developmental biology, Rockefeller Institute, will present "Problems of Specificity in the Development and Functioning of the Nervous System."

Hospital Panel on Medical Genetics.—The Adelphi Hospital medical staff will present a panel meeting on medical genetics, Wednesday, Nov. 25, at the new auditorium. Dr. Alexander S. Wiener, Brooklyn, will moderate the panel and present "Hereditary Disorders of the Blood." Dr. Victor A. McKusick, Baltimore, will give "Hereditary Disorders of Connective Tissue" and Dr. Franz J. Kallmann, will present "Hereditary Disorders of the Nervous System." For information, write the Adelphi Hospital, 50 Greene Ave., Brooklyn 38.

Annual Lecture on Skin Diseases.—The department of dermatology and syphilology of the New York University Post-Graduate Medical School announced the ninth annual Sigmund Pollitzer Lecture to be given by Prof. Harold F. Blum Nov. 17, 8 p. m., in Classroom B of Alumni Hall, 550 First Ave. Professor Blum, physiologist at the National Cancer Institute and visiting professor at Princeton University, will present "Carcinogenesis by Ultraviolet Light: Experiment and Interpretation." The Pollitzer Lectures are made possible by a grant from Mrs. Sigmund Pollitzer, who established the lectureship in honor of her husband, the late Dr. Sigmund Pollitzer, former professor of dermatology and syphilology at the Post-Graduate Medical School. Under the terms of the grant, "outstanding" scientists and teachers are invited to speak in selected subjects relating to skin diseases.

Grants for Research.—On the recommendation of the Health Research Council, the New York City Board of Estimate on Oct. 8 approved 14 medical research grants which will total $1,023,309 over a five-year period. Under the terms of the grants, $270,713 will be spent in the first year, the remaining $752,596 in the following four years. Grants were made to medical schools in New York City for research work on specific projects to be conducted in five municipal hospitals. In addition, newly created "New York City Investigatorships" were awarded to six young university scientists who will do research work in municipal hospitals. The grants to the medical schools will support both laboratory and clinical research in cancer, infectious diseases, narcotic addiction, disorders of metabolism, and diseases of the cardiovascular system, central nervous system, and pulmonary system. The Health Research Council was set up by Mayor Wagner in September, 1958, "to work out policy and guide the City in allocating city funds which will enable scientists to carry on research work in health and medical problems." Dr. Walsh McDermott, Livingston Farrand Professor of Public Health and Preventive Medicine at Cornell University Medical College, is chairman of the council. The grants voted by the Board of Estimate are the first to be made under the program.

OHIO

Fellowships in Industrial Medicine.—The University of Cincinnati's Institute of Industrial Health is offering graduate fellowships in industrial medicine. The institute, in the College of Medicine, provides professional training for graduates of approved medical schools who have completed at least one year of internship. The three-year program leading to the degree of doctor of industrial medicine satisfies the requirements for certification in occupational medicine by the American Board of Preventive Medicine. Two years are devoted to intensive academic and clinical study in industrial medicine. A third year is spent in residency in an industrial medical department or in some comparable organization. Stipends for the first two years are from $3,000 to $4,000, depending upon marital status. In the final or residency year the fellow is compensated by the organization in which he is completing his training. Two other programs are offered to qualified applicants: a one-year course, to applicants who wish to become candidates for the degree of master of science; and a three-year academic program leading to the degree of doctor of science, to those who wish to pursue careers in teaching and research. Fellowship stipends are available in these programs. For information, write: Secretary, Institute of Industrial Health, College of Medicine, Eden and Bethesda Avenues, Cincinnati 19.

OKLAHOMA

Dr. Donahue Resigns as Mental Health Director.—Dr. Hayden H. Donahue, Oklahoma City, director of the Oklahoma Department of Mental Health for the past seven years, announced his resignation on Aug. 4, "to seek a residency in psychiatry, do mental health research, and complete the writing of a book." It has been reported that Dr. Donahue has accepted the position of assistant director, Arkansas State Hospital, Little Rock. Governor J. Howard Edmondson issued a proclamation stating: "Primarily under the director of Dr. Hayden H. Donahue, Oklahoma Mental hospitals and schools for the retarded have risen . . . to a position reflecting dignity, pride and national pre-eminence." The proclamation declared Sept. 22 as Donahue Appreciation Day and a testimonial dinner was held on that date with Governor Edmondson as the principal speaker and Dr. George H. Guthrey, Oklahoma City, as master of ceremonies.

PENNSYLVANIA

Philadelphia

Dinner for Hospital Alumni.—The 73rd annual dinner of the Association of Ex-Residents and Resident Physicians of the Philadelphia General Hospital will be held on Tuesday, Dec. 1, at 7 p. m., at Williamson's Presidential Dining Rooms, Presidential Apartments, City Line and Schuylkill Expressway, Philadelphia. All members are urged to attend. For information, write Dr. William W. Wilson, Secretary-Treasurer, 133 S. 36th St., Philadelphia 4.

University News.—The University of Pennsylvania held a special convocation to commemorate the 75th anniversary of the founding of the School of Veterinary Medicine Oct. 3. The convocation was scheduled to coincide with the 77th annual convention of the Pennsylvania State Veterinary Medical Association.—A group of 37 Italian physicians were guests of the Temple University Medical Center Aug. 23. The doctors, all professors of medical schools in Italy, toured medical centers in the United States and Canada.

Dr. Nichols Appointed Department Head.—The appointment of Dr. Henry T. Nichols as professor and head of the department of thoracic surgery was confirmed by the board of trustees of Hahnemann Medical College and Hospital. Dr. Nichols had been acting head of the department since September, 1958. A member of the American Board of Surgery and the Board of Thoracic Surgery, Dr. Nichols is affiliated with the Veterans' Administration Hospital, Rolling Hill Hospital (Jenkintown), Albert Einstein Medical Center and Womans' Hospital.

Research Laboratory Dedicated.—On Sunday, Sept. 20, a new research laboratory of Wills Eye Hospital, headed by Dr. Irving H. Leopold, was dedicated. The principal address will be delivered by Governor David L. Lawrence of the Commonwealth of Pennsylvania. The research department of the Wills Eye Hospital was formally initiated in 1950. Through a Ford Foundation contribution and matching National Institutes of Health funds and other contributions, the new laboratory building was made possible. There are 26 full-time research workers, in addition to members of the hospital staff who engage in part-time research. The new building is equipped with departments of pathology, microbiology, biochemistry, pharmacology, and radioactive isotopes. The laboratory is an unendowed department that must depend on new grants and the support of friends for its maintenance.

RHODE ISLAND

Medical History Meeting.—The Benjamin Waterhouse Medical History Society will meet in combination with the Providence Medical History Society at the Rhode Island Hospital Monday, Nov. 16. Dr. Charles W. Robertson, associate professor of surgery, Boston University School of Medicine, will be speaker, presenting "Some Observations on Presidential Illnesses." For information, write Dr. John J. Byrne, 818 Harrison Ave., Boston 18, Secretary (KE 6-8600).

VERMONT

Dedicate New Medical Building.—A program of dedication for the new medical building at the University of Vermont College of Medicine, Burlington, was held Sept. 24-26 in celebration of completion of the first phase of the proposed building program. The new building, the first to be built in nearly 55 years, provides new and expanded research facilities. The first medical building for the college, Pomeroy Hall, dedicated in 1829, is still used by the university for offices and classrooms. A symposium, "Peptic Ulcer," Sept. 24, was opened by Dr. George A. Wolf Jr., dean of the college of medicine. On Sept. 25, medical grand rounds were held and the first annual Beaumont Lecture, "Gastric Research in the Hundred Years Since Beaumont," was given by Dr. Stewart Wolf, professor of medicine, University of Oklahoma, Oklahoma City. At the dedication ceremonies, Sept. 16, Dr. Ernest M. Allen, chief, division of research grants, National Institutes of Health, United States Public Health Service, presented an address.

WASHINGTON

State Medical Election.—The Washington State Medical Association elected the following 1959-1960 officers: president, Dr. Frederick A. Tucker, Seattle; president-elect, Dr. Homer W. Humiston, Tacoma; immediate past-president, Dr. Emmett L. Calhoun, Aberdeen; vice-president, Dr. Edward C. Guyer, Seattle; secretary-treasurer, Dr. Wilbur E. Watson, Seattle; and speaker, House of Delegates, Dr. Dean K. Crystal, Seattle. The executive secretary is Mr. Ralph W. Neill, 1309 Seventh Ave., Seattle 1.

WISCONSIN

Rehabilitation Center Opens.—The University of Wisconsin Medical Center's Respiratory and Rehabilitation Center, aimed at "restoration of disabled patients to the greatest possible physical, mental, social, and vocational capacity," began serving the state Sept. 11. The center is located in the remodeled seventh floor of University Hospitals, Madison, where opening of the new facility was observed at brief ceremonies the afternoon of Sept. 11. A Wisconsin physician may refer to the center any patient with a severely disabling disease or injury which demands long-term reorganization of the patient's life. Dr. Arthur Siebens, director, and Dr. W. Theodore Bruns, assistant director, will be responsible for treating the medical problems and guiding the staff teamwork. The center has an orthotist to design, adapt, and make devices for the patient. Aid from the university department of clinical psychology and the Speech and Hearing Clinic will be available. The facility is also concerned with basic research and studies relating to the mechanics and measurement of breathing. The third major purpose of the center is teaching. Several staff members are on the Medical School faculty and will teach in their respective fields. The new facility is supported by funds from the State of Wisconsin and organizations such as the National Foundation, the Sister Elizabeth Kenny Foundation, the Benjamin Wishner Estate, the Bess Heath Estate, the United Fund of Marathon County, and the Oscar Mayer Foundation of Madison.

GENERAL

Dr. Wilson Becomes Tuberculosis Director.—Dr. Julius L. Wilson became full-time director of medical education for the National Tuberculosis Association and its medical section, the American Trudeau Society, as of Oct. 1. For the past six years Dr. Wilson has been serving as part-time director of medical education while serving also as director of the Henry Phipps Institute for the Study and Prevention of Tuberculosis of the University of Pennsylvania, Philadelphia.

Meeting on Cerebral Palsy in Los Angeles.—The American Academy for Cerebral Palsy will meet at the Statler-Hilton Hotel, Nov. 30-Dec. 2. Instructional courses and question-and-answer luncheons will be held Nov. 30 and Dec. 1. Dr. Alvin J. Ingram, Memphis, Tenn., will give the presidential address the morning of Dec. 1. A research afternoon is planned for Dec. 1, with seven papers scheduled, including discussion periods. Round-table discussions will be conducted the morning of Dec. 2. Scientific exhibits are planned.

Western Surgical Meeting.—The 67th annual meeting of the Western Surgical Association will be held Nov. 19-21 at the Broadmoor Hotel, Colorado Springs, Colo. A total of 36 papers is scheduled to be presented at the four scientific sessions. Dr. James T. Priestley, Rochester, Minn., will present "Surgery, Science, and Education" as the president's address the morning of Nov. 20. The annual banquet is planned for the evening of Nov. 20. A ladies' program is arranged. For information, write Dr. John T. Reynolds, 612 N. Michigan Blvd., Chicago 11, Secretary.

Meeting on Psychoanalysis.—The scientific sessions of the midwinter meeting of the Academy of Psychoanalysis will be held Dec. 5-6, 9 a. m. to 5 p. m., at the Hotel Roosevelt, New York City. The theme of the first day's meeting will be "Psychoanalytic Concepts in Allied Fields." Harold Lasswell, Ph.D., will speak on the implications psychoanalytic concepts have for political science; Weston LeBarre, Ph.D., on the implications for anthropology; and Talcott Parsons, Ph.D., on the implications for social science. The second day's meeting will be devoted to a series of clinical papers by members of the academy. The address of the academy is 125 E. 65th St., New York 21.

Propose Health and Research Year.—The governments of the American Republics, plus those of France, The Netherlands, and the United Kingdom went on record as supporting the establishment of an International Health and Medical Research Year. The action came during a session of the 11th annual meeting of the Pan American Health Organization's directing council. Meeting also as the regional committee for the Western Hemisphere of the World Health Organization, the council's vote goes to WHO Director-General M. G. Candau in Geneva. U. S. Surgeon General Dr. Leroy E. Burney presented the resolution favoring the year on behalf of his delegation.

Conference on Electrical Techniques in Medicine.—The 12th annual Conference of Electrical Techniques in Medicine and Biology will be held Nov. 9-12 at the Hotel Sheraton, Philadelphia. Besides two general sessions, special sessions are arranged under the following titles:

Ultraviolet Radiation
Cardiovascular
Microwave Radiation
Ultrasonic Radiation
Infrared Radiation

An exhibition and demonstration of electrical medical equipment and accessories is planned. More than 40 papers will be presented at the special sessions, and more than 20 additional papers will be concerned with cardiovascular techniques and instrument advances in biomedical electronics. Chairman of the conference committee is Herman P. Schwan, Ph.D., Philadalephia. Advanced registration is $5. A program of tours is planned.

List of Western Meetings.—Starting in November, the *Rocky Mountain Medical Journal* will publish monthly a bulletin entitled "What goes on." Physicians in the following states will receive the publication: Alaska, Arizona, Colorado, Idaho, Montana, Nevada, New Mexico, Oregon, Utah, Washington, and Wyoming. The medical societies in these states are cooperating in the project. "What goes on" will list medical meetings and special lectures of interest in an effort to keep physicians informed of area postgraduate education opportunities. It will also include notification regarding postgraduate sessions offered by medical schools as well as speakers sponsored by hospitals, specialized medical organizations, and area medical societies. Listings will be grouped by geographical divisions for the month covered by the particular issue. A separate section will carry future dates. "What goes on" is sponsored by Lederle Laboratories, a division of the American Cyanamid Company, and is being sent free to all physicians in the 11-state region.

Travel Grants for Congress of Endocrinology.—The first International Congress of Endocrinology will be held in Copenhagen, Denmark, July 18-23, 1960. The Endocrine Society has obtained funds to provide a limited number of allotments in support of travel to the congress for scientists residing in the United States and Canada who may require such assistance. Individual allotments will not exceed $750 each. Application for travel allotment should be submitted in duplicate in the form of a letter giving information on age, training, publications, academic or professional title, and society affiliation. Applicants who plan to submit papers for presentation at the congress should include the proposed title of each paper. Such letters should be submitted before Nov. 15 and should be addressed to Dr. Henry H. Turner, Secretary, The Endocrine Society, 1200 North Walker, Oklahoma City 3, Okla. Applicants will be responsible for their own passports, registration, travel arrangements, and hotel reservations. For information on registration and submission of papers, write The Secretariat, Hormonafdelingen, Statens Seruminstitut, Copenhagen.

Meeting of Northwest Physicians.—The American College of Physicians Pacific Northwest Region meeting for Oregon, Washington, and British Columbia will be held Nov. 20-21 at the Sheraton Hotel, Portland, Ore. Of the papers scheduled for presentation, the following include invited authors:

Congestive Failure Due to Auricular Fibrillation: A Twenty-Five-Year Follow-up, Dr. Isidor C. Brill, and Dr. Edward E. Rosenbaum, Portland.
Mortality in Myocardial Infarction in the Older Age Group, Dr. Llewellyn N. Roberts, Victoria, B. C.
Auscultatory Implications of the Split Second Heart Tone, Dr. Charles P. Wilson, and Dr. Marvin J. Weinstein, Rochester, Minn.
Evaluation of Pulmonary Function, Dr. Donald M. Pitcairn, Portland.
The Incidence of Obstructive Pulmonary Disease in Chronic and Custodial Tubercular Patients, Dr. Carroll J. Martin, and Dr. Wilbur Hallett, Seattle.
Malabsorption in Gastrocolic Fistula, Dr. John A. Benson Jr., Boston.
Newer Tests for Diagnosis of Acquired Hemolytic Anemia, Dr. Bernard Pirofsky, Portland.

At the dinner the evening of Nov. 20, Dr. Howard P. Lewis, Portland, president of the college, will present an address. For information, write the American College of Physicians, 4200 Pine St., Philadelphia 4.

Psoriasis Research Award.—The department of dermatology, Baylor University College of Medicine, Houston, Texas, announced the Mr. and Mrs. J. M. Taub International Memorial Award for Psoriasis Research. This annual award of $1,000 was established in 1957, by Carol and Henry J. N. Taub in honor of their grandparents, Mr. and Mrs. Henry J. N. Taub. The award is designated for the individual or group who has done the "most outstanding investigative work" in this field. Results of the research must have been presented before a dermatological medical society or published in one of the recognized medical journals during the calendar year. The name of any applicant for the award, together with supporting data, should be submitted for consideration by Dec. 31 of the same year. The recipient will be determined by a committee composed of Drs. Marcus R. Caro, Chicago; Edward P. Cawley, Charlottesville, Va.; Arthur C. Curtis, Ann Arbor, Mich.; Eugene M. Faber, San Francisco; John M. Knox, Houston, Texas; Aaron B. Lerner, New Haven; and Carl T. Nelson, New York City. If in the opinion of the committee a given calendar year fails to yield a deserving contribution, the award will not be given. Address all communications to Dr. John M. Knox, Department of Dermatology, Baylor University College of Medicine, Houston 25, Texas.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

	Oct. 10, 1959		Oct. 11, 1958
Area	Paralytic Type	Total Cases	Total
New England States			
Maine	14	14	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	4	7	2
Rhode Island	..	..	..
Connecticut	3	3	3
Middle Atlantic States			
New York	15	20	16
New Jersey	7	8	17
Pennsylvania	2	2	7
East North Central States			
Ohio	6	12	19
Indiana	3	6	9
Illinois	9	19	10
Michigan	6	14	98
Wisconsin	1	2	3
West North Central States			
Minnesota	14	15	4
Iowa	9	16	..
Missouri	9	14	15
North Dakota	..	..	3
South Dakota	..	..	..
Nebraska	2	7	3
Kansas	3	3	3
South Atlantic States			
Delaware	..	..	1
Maryland	4	4	1
District of Columbia	..	..	..
Virginia	10	10	12
West Virginia	12	12	17
North Carolina	16	16	..
South Carolina	3	3	1
Georgia	3	3	3
Florida	2	3	12
East South Central States			
Kentucky	4	6	4
Tennessee	11	14	8
Alabama	4	4	1
Mississippi	1	1	3
West South Central States			
Arkansas	8	21	..
Louisiana	..	4	4
Oklahoma	1	2	..
Texas	10	16	16
Mountain States			
Montana	..	..	1
Idaho	..	1	..
Wyoming	..	..	1
Colorado	1	2	1
New Mexico	..	..	1
Arizona	3	3	2
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	7	7	9
Oregon	6	8	..
California	12	13	9
Alaska	4	5	..
Hawaii	..	..	2
Territories and Possessions			
Puerto Rico	..	..	..
Total	229	320	321

Report on Married Couples.—The Metropolitan Life Insurance Company reported that currently the United States has about 39½ million married couples. In almost one-half of them the husband is 25 to 44 years old. According to the Bureau of Census, the total number of married couples increased by 10⅔ million from 1940 to 1958. Nearly the same growth is expected in the like period ahead, with a total of about 50⅓ million married couples by 1975. The rising tide of young people and the high marriage rates of the postwar years have produced an increase of about 50% from 1940 to 1958 in the number of couples with husbands under 25 years of age. The reported outlook is that the number of such young couples will more than double from 1958 to 1975, reaching a total of about 4.7 million. The number of couples with husbands at age 65 or older mounted by 73% from 1940 to 1958, with a further increase of 36% expected by 1975. This growth reportedly reflects the aging of the population. For couples in which the husband is 25-44 years of age, the increase between 1940 and 1958 averaged about 30%. Couples headed by husbands in midlife have been increasing and are expected to continue to do so.

Smallpox Declining in the Americas.—Smallpox cases reported in the Americas dropped fourfold during the past decade, according to a report presented before the directing council of the Pan-American Health Organization. While 18,352 cases were reported in the Americas during 1949, only 4,311 were reported last year. Yet smallpox is still a major public health problem in the hemisphere, says the report. During this 10-year period, of the total of 103,491 cases reported in 15 countries and other areas, there were at least 16,000 deaths. The directing council urged all countries of the Americas to "... accord the smallpox eradication program the importance and priority it deserves, from the viewpoint of both national and international health." The 15th Pan American Sanitary Conference, held last year in San Juan, Puerto Rico, declared smallpox a health problem requiring the attention of all countries and requested that necessary measures be taken for the eradication of the disease from the hemisphere. Since 1948 PASB has spent about $350,000 in aiding the governments of the hemisphere in combatting smallpox. The 90 member States of the World Health Organization, meeting during the 12th World Health Assembly in Geneva, voted to make the smallpox eradication campaign global earlier this year.

National Index on Deafness, Speech, and Hearing—Gallaudet College, Washington, D. C., and the American Speech and Hearing Association established a National Index on Deafness, Speech, and Hearing. This index will combine the present indexing and abstracting functions of the Central Index of Research on the Deaf at Gallaudet College and the projected indexing and abstracting functions of the American Speech and Hearing Association. The general policies of the national index will be formulated by a committee composed of representatives of Gallaudet College and representatives of the Association. The index, to be located at Gallaudet College, will be directed by Stephen P. Quigley, Ph.D., Washington, D. C. The purpose of the index is "to index and abstract all professional literature pertaining to deafness, speech and hearing and to make this material readily available to all interested persons." Present and future literature will be included as will the relevant past literature. The index will make the collected material available through a regular, professional publication. The National Index on Deafness, Speech and Hearing is made possible in part by a grant from the Office of Vocational Rehabilitation of the Department of Health, Education, and Welfare. For information, write Stephen P. Quigley, Ph.D., Director, National Index on Deafness, Speech and Hearing, Gallaudet College, Washington 2, D. C.

Fellowships for Residents in Pediatrics.—The American Academy of Pediatrics will grant 28 or more fellowships to pediatric residents for the year beginning July 1, 1960, and covering a period of six months to one year. These fellowships, created to enable young physicians, who are legal residents of the United States or Canada and who are in financial need, to complete their pediatric training, have been provided in two groups. Mead Johnson & Company, has made possible the awarding of 18 or more fellowships to carry a stipend of from $500 to $1,000 each, depending on the need and the length of time required to complete training. A second group of 10 fellowships, each carrying a stipend of $500 and awarded on the same basis as the others, has been made available through a grant to the academy from the Gerber Baby Food Foundation. Requirements for the awards are (1) a letter from the chief of service indicating that the individual will have completed by July 1, 1960, one year of pediatric training credited by the American Board of Pediatrics; that the resident has performed his work ably; and that there is need for financial assistance; (2) a letter from the resident requesting the fellowship stating that he intends to enter pediatric private practice at the conclusion of his residency training. Those interested in applying may correspond with the American Academy of Pediatrics, 1801 Hinman Ave., Evanston, Ill. The deadline for the receipt of applications will be Feb. 15.

Fund to Aid Interns and Residents.—A $400,000 George W. Merck Memorial Loan Fund has been established by the Merck Company Foundation "to help meet an important need for financial aid to interns and residents." The fund will assist "deserving interns and residents to seek the best possible postgraduate training in teaching hospitals before entering practice." It is estimated that 60 to 100 young doctors will benefit each year from the fund. The 18 medical schools participating are associated with the following universities: Boston, California, Chicago, Columbia, Cornell, Harvard, Illinois, Johns Hopkins, New York, Northwestern, Pennsylvania, St. Louis, Tufts, Vanderbilt, Vermont, Virginia, Washington (St. Louis), and Yale. They were selected on the basis of close personal friendships which the late George W. Merck had with members of their faculties or staffs. Graduates of other medical schools also may be eligible for loans if they take the internship or residency at any of the 48 teaching hospitals affiliated with the participating schools. Administration of the fund will be by the deans of the medical schools. The Merck Company Foundation will allocate the $400,000 over a period of eight years, by which time the fund is expected to be self-sustaining. Initial payments to the 18 schools have been completed, so that funds will be available in 1959. The Merck Company Foundation is a nonprofit corporation supported by Merck & Co., Inc. It makes contributions to education and other causes.

Society News.—The **American Congress of Physical Medicine and Rehabilitation** elected the following officers for 1959-1960: Dr. Frederic J. Kottke, Minneapolis, president; Dr. Donald A. Covalt, New York City, president-elect; Dr. Donald J. Erickson, Rochester, Minn., first vice-president; Dr. Jerome S. Tobis, New York City, second vice-president; Dr. Louis B. Newman, Chicago, third vice-president; Dr. Charles D. Shields, Washington, D. C., fourth vice-president; Dr. William J. Erdman, II, Philadelphia, fifth vice-president; Dr. Frances Baker, San Mateo, Calif., secretary; Dr. Frank H. Krusen, Rochester, Minn., treasurer; Dr. Walter J. Zeitel, Cleveland, executive director; and Dr. Glenn Gullickson Jr., Minneapolis, assistant to the executive director. Miss Dorothea C. Augustin, Chicago, is executive secretary.——For the year Sept. 12, 1959, to Sept. 10, 1960, the following are the officers of the **American Association of Obstetricians and Gynecologists:** president, Dr. Robert A. Ross, Chapel Hill, N. C.; president-elect, Dr. John L. Parks, Washington, D. C.; vice-president, Dr. Emmett D. Colvin, Atlanta, Ga.; secretary, Dr. Clyde L. Randall, Buffalo; assistant secretary, Dr. Clayton T. Beecham, Philadelphia; and treasurer, Dr. Harold L. Gainey, Kansas City, Mo.——At the annual meeting of the **American Association of Medical Clinics** the following were elected: Dr. Russel V. A. Lee, Palo Alto, Calif., president; Dr. Harold D. Caylor, Bluffton, Ind., first vice-president and president-elect; Dr. Bernard A. Watson, Clifton Springs, N. Y., second vice-president; and Dr. Joseph B. Davis, Davis Clinic, 131 N. Washington St., Marion Ind., secretary-treasurer.

Survey of Surgery.—The Metropolitan Life Insurance Company reported that well over 10 million surgical operations are performed in this country each year, according to the National Health Survey program of the U. S. Public Health Service. No less than 60% of all patients in short-stay hospitals receive surgical treatment. The scope of surgery has broadened, especially in the last two decades, and the risk of operation has lessened. In a review of the experience of one large hospital, covering more than 100,000 operations and anesthetic procedures of all types during 1945-1954, the surgical mortality was 43% below that of 1925-1934. Reductions in the mortality associated with a number of specific operations were reported in a St. Louis study. There was a decline of 88% between the two periods 1916-1938 and 1948-1952 in the surgical mortality of one type of operation for gallbladder disease. About as rapid was the decline from 1920 to 1953 for thyroid operations in cases of toxic goiter. Within a period of 15 years, a drop of nearly 85% was reported for closure of perforated peptic ulcers. Other operations with reductions in surgical risk in this St. Louis study were corrections of obstructions of the small intestine, partial gastric resection in duodenal ulcer, esophagectomy in cancer, and radical mastectomy. Advances in cardiac surgery were illustrated by a study of several Boston hospitals with patients having a mitral valvuloplasty. Among patients with some impairment of function or with progressive symptoms due to the disease, the rate of 14% in 1949-1951 was cut to 4% in 1951-1953. Subsequently the surgical mortality dropped to less than 1% for the patients in the study who had the operation in 1953-1956.

Report on Medical Manpower.—The ratio of physicians to population in the United States, which has ranged between 131 and 135 per 100,000 persons for 20 years, "will drop to 126 per 100,000 by 1975 unless the rate of graduating students increases substantially," a report issued by the Public Health Service indicates. The number of dentists per 100,000 persons in the population will decline even more sharply, the report states. Entitled "Health Manpower Source Book, Section 9: Physicians, Dentists, Nurses," the report reveals trends in the education, location, and specialization of these professional personnel. In the academic year 1958-1959, the 85 medical schools in the United States graduated 6,895 physicians. To maintain the present physician-population ratio, U. S. medical schools reportedly would need to graduate about 10,360 students by 1975—nearly 3,000 above the 7,410 graduates currently predicted for that year. The 47 dental schools in the United States graduated 3,083 dentists in the academic year 1957-1958. Despite the addition of eight new dental schools since World War II and large increases in the number of graduates, the ratio of dentists to population remains below pre-World War II levels. According to the report, the ratio of dentists was 62 per 100,000 in 1940, 57 in 1958, and is expected to decline to about 50 per

100,000 in 1975. There should, however, be an increase in the ratio of professional nurses—from 268 per 100,000 population in 1958 to 284 per 100,000 in 1970, the report indicates. The nurse-population ratio has increased almost fivefold in the United States since 1910. In the academic year 1957-1958, the 1,145 schools of nursing in the United States enrolled about 113,000 students and graduated 30,410 nurses. The report also contains information about doctors of osteopathy. The current combined ratio of doctors of medicine and osteopathy to population is about 140 per 100,000 persons and "this is expected to decline to 133 per 100,000 by 1975." The report, listed as Public Health Service Publication No. 263, Section 9, may be purchased from the Superintendent of Documents, Government Printing Office, Washington 25, D. C., at 50 cents per copy. Single free copies may be obtained from the Division of Public Health Methods, Public Health Service, Washington 25, D. C.

CANADA

Dr. McRae Receives Radiology Medal.—Dr. Donald L. McRae, Montreal, associate professor of radiology, McGill University, received the Caldwell Lecture Medal of the American Roentgen Ray Society following presentation of the Caldwell Lecture during the 60th annual meeting of the society. The title of Dr. McRae's address was "The Significance of Abnormalities of the Cervical Spine." The Caldwell Lecture honors the late Dr. Eugen W. Caldwell, pioneer user of radiation in medicine. Dr. McRae is the first Canadian to present the Caldwell Lecture.

FOREIGN

Congress on Audiology in Bonn.—The fifth congress of the International Society of Audiology will be held Sept. 28-Oct. 1, 1960, at Bonn, German Federal Republic. Three round-table discussions are arranged: the cortical auditory function and its disturbances in adults and in children; physiology, functional pathology, and clinical significance of recruitment; and adaptation and related phenomena —their clinical significance. Free communications are planned. The official languages will be German, French, English, and Spanish with simultaneous translation. For information, write the General Secretary, International Society of Audiology, 4, Rue Montvert, Lyon, France.

Civil Defense Conference Postponed.—The fourth International Civil Defense Conference, which was to be held in Paris Sept. 28-Oct. 3, as well as the first International Exhibition of Civil Defense Equipment, have been postponed. During discussions in Paris, "objections were raised regarding some of the items on the agenda, i. e., the functioning of the World Radioactivity Warning Centre, set up in Geneva in November, 1958." Since the preparatory work for the fourth International Civil Defense Conference had been completed at the time of its cancellation, the executive bureau is taking steps to organize the conference and exhibition at a date and in a place which will be fixed subsequently and will be chosen to suit the participants already registered.

Congress on Medical Photography.—The medical section of the Deutsche Gesellschaft für Photographie eV. (DGPh), Cologne, Germany, announced that, contrary to previous information, the first International Congress on Medical Photography and Cinematography will take place Sept. 27-30, 1960, in connection with the "photokina" (Sept. 24-Oct. 2) at Cologne. Purpose of the congress will be to show the present status of photographic and cinematographic exposure and reproduction technique in medicine. Purely medical problems and complexes are not subject to discussion. Deadline for the registration of lectures is March 15, 1960. Deadline for the registration of persons is Aug. 1, 1960. The program will be available in May, 1960. For information, write Deutsche Gesellschaft für Photographie eV. Neumarkt 49, Köln, Germany.

Air Pollution Conference Held in London.—North America's Air Pollution Control Association met with air pollution control groups representing countries from the other five continents in London Oct. 20-23 at the world's first International Clean Air Conference. The world-wide conference commemorated the 75th anniversary of the British Commonwealth's organized effort to promote clean air and the 60th anniversary of Great Britain's National Society for Clean Air. Chairman of the conference was Sir Hugh Beaver, English industrialist. The purpose of the international conference was to exchange information and promote international cooperation in the practical aspects of air pollution prevention and control. Subjects included international cooperation, research information exchange, and education in public relations phases of air pollution control.

Festival of Scientific Films in Paris.—The opening of the seventh session of the Permanent International Festival of Medico-Surgical and Scientific Motion Pictures, organized by La Gazette Medicale de France in cooperation with the National Association of the Motion Picture Producer Doctors and Scientists of France, will take place in Paris, Feb. 17, 1960, at the Faculte de Medecine. The producers of medicosurgical or scientific films of 16 mm. substandard format (exclusively) not shown in France before who wish to participate in this event should send their productions before Dec. 5, the date of the meeting of the Technical Council in charge of selecting the films, to the Association Nationale des Medecins Cinéastes et des Cinéastes

Scientifiques de France, 23 Boulevard de Latour-Maubourg, Paris 7e. Foreign participants would find it advantageous to send their material through the cultural attache of their embassy in Paris, via their department of foreign affairs.

Pathology Meeting in London.—A meeting of the International Academy of Pathology will be held at the Royal College of Surgeons of England, Lincoln's Inn Fields, London, W. C. 2, England, June 20-24, 1960. The presentations will consist of the following: papers on June 20; on June 21 a slide seminar, "Proliferative Lesions of Breast," with professors C. Oberling of France, Robert W. Scarff, of London, and Lauren V. Ackerman, of St. Louis, as moderators; on June 22 an all-day symposium, "Pathophysiology and Pathology of the Kidney," by invited speakers; on June 23 and 24 a joint meeting of the American and British pathologists with a symposium on thyroiditis and cancer of the thyroid. Scientific exhibits will be accepted and visits to research centers will be arranged. There will be a social program for pathologists and their wives. For information, write Dr. Fathollah K. Mostofi, Secretary, International Academy of Pathology, Armed Forces Institute of Pathology, Washington 25, D. C.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, July 8. Final date for filing application is January 8. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. New Haven, Nov. 14-16. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part II.* Chicago. Jan. 19-21, 1960. The deadline for the receipt of application was Aug. 15. *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications is Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Pathology: New Orleans, Nov. 12-14. Final date for filing application was October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pathology: *Examination in Forensic Pathology.* New Orleans, Nov. 13. Final date for filing application is October 1. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

American Board of Pediatrics: *Oral.* Washington, Dec. 4-6. *Written.* Jan. 8. Final date for filing application for the written examination is Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application was July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Closing date for filing applications was August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Oral examinations (Part II):* Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral-Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Abbott, John Steele Ⓜ St. Paul, Minn.; University of Pennsylvania Department of Medicine, Philadelphia, 1908; served with the American Expeditionary Forces during World War I; formerly assistant professor of surgery at the University of Minnesota Medical School; past-president of St. Paul Surgical Society; from 1909 to 1912 assistant in surgery at the Mayo Clinic in Rochester, Minn.; retired from the Veterans Administration on April 30, 1956; formerly associated with the Ancker Hospital, Miller Hospital, and St. Luke's Hospital, where he died Aug. 10, aged 75.

Adams, William Bradford, Owls Head, Maine; Harvard Medical School, Boston, 1918; specialist certified by the American Board of Pediatrics; member of the American Academy of Pediatrics; veteran of World War I; formerly practiced in Springfield, Mass., where he was associated with the Shriners' Hospital for Crippled Children, Health Department Hospital, and Wesson Maternity Hospital; died Aug. 16, aged 69.

Anderson, Stewart Harry Ⓜ Kerrville, Texas; University of Illinois College of Medicine, Chicago, 1915; veteran of World War I; served on the staff of the Veterans Administration Hospital; died in the Sid Peterson Memorial Hospital Aug. 3, aged 69.

Armington, Herbert Hamlin Ⓜ Providence, R. I.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; at one time school physician; formerly staff member of the Providence Lying-in Hospital and the Rhode Island Hospital; died in the Veterans Administration Hospital Aug. 11, aged 81.

Baron, Benzion Chaim Ⓜ Munising, Mich.; Northwestern University Medical School, Chicago, 1930; formerly member of the board of education; past-president of the Munising Rotary Club; veteran of World War II; on the staff of Munising Hospital; died in Palmer Aug. 3, aged 53.

Bartruff, Charles Henry Ⓜ Reinbeck, Iowa; Drake University College of Medicine, Des Moines, 1913; served overseas during World War I; staff member of the Grundy County Memorial Hospital in Grundy Center; died Aug. 24, aged 71.

Bassler, Anthony Ⓜ New York City; born in New York City May 24, 1874; Bellevue Hospital Medical College, New York City, 1898; successively lecturer in pediatrics, pathology, and internal medicine at his alma mater from 1900 to 1910; for many years on the faculty at New York Polyclinic Medical School and Hospital and Fordham University School of Medicine; specialist certified by the American Board of Internal Medicine; first chairman and founder in 1917-1918 of the Section on Gastroenterology, American Medical Association; past-president of the National Gastroenterological Association, National Society for the Advancement of Gastroenterology, New York Gastroenterological Association, American Physicians Art Association, and the New York City Physicians Golfing Association, of which he was one of the founders; served as American president of the International Society of Gastroenterology, which he helped organize, for which France gave him the Legion of Honor, and president of the American delegation to the International Congress on Hepatic Insufficiency in Vichy, France, in September, 1937; an honorary vice-president of the American Society of Stomatology; member of the American College of Gastroenterology, of which he was one of the founders and first president, the Endocrine Society, and the American Roentgen Ray Society; fellow of the American College of Physicians; honorary member of the Belgium Gastroenterological Society; cited by the Navy for his work on dysentery in World War I; also cited by the Army for his aid to the Selective Service; consultant in gastroenterology, Doctors, Misericordia, and St. Vincent's hospitals and New York Polyclinic Medical School and Hospital in New York City, St. John's Riverside Hospital, Yonkers, St. Agnes Hospital, White Plains, United Hospital, Port Chester, New Rochelle (N. Y.) Hospital, and the Yonkers Professional Hospital in Yonkers; co-editor of the *Review of Gastroenterology* which dedicated its November-December, 1939, issue to him in honor of his sixty-fifth birthday; on June 9, 1938, received the honorary degree of doctor of laws from the Hahnemann Medical College of Philadelphia; author of books in his speciality and contributed much to periodic literature; collaborator in fine systems of medicine; died Aug. 20, aged 85.

Bell, Aaron Ⓜ New York City; Cornell University Medical College, New York City, 1926; specialist certified by the American Board of Psychiatry and Neurology, Inc.; member of the American Academy of Neurology and the Association for Research in Nervous and Mental Disease; psychiatrist of the New York State Department of Mental Hygiene; served as director of neuropsychiatry at Lenox Hill Hospital and as consulting neurologist at the Huntington (N. Y.) and Hasbrouck Heights (N. J.) hospitals; died Aug. 26, aged 57.

Ⓜ Indicates Member of the American Medical Association.

Benefield, Charles Edward Ⓜ Fort Smith, Ark.; Memphis (Tenn.) Hospital Medical College, 1902; died Aug. 6, aged 88.

Bixby, Edward Welles Ⓜ Wilkes-Barre, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1911; fellow of the American College of Physicians; member of the American Trudeau Society; past-president of the Luzerne County Medical Society; served in France during World War I; served on the staffs of the Wilkes-Barre General Hospital and the White Haven (Pa.) Sanatorium; died at Glen Summit Aug. 21, aged 73.

Blake, Albert Julian Ⓜ Paterson, N. J.; Harvard Medical School, Boston, 1937; interned at St. Joseph's Hospital; served a residency at the Hopedell Hospital in Preakness, N. J.; veteran of World War II; an examining physician in Paterson's public schools; on the courtesy staff of the Barnert Memorial Hospital, where he died Aug. 24, aged 48.

Blakeley, Arthur C. Ⓜ Detroit; Detroit College of Medicine, 1911; associated with the Veterans Administration; died Aug. 20, aged 75.

Blum, Samuel George, Brooklyn; Cornell University Medical College, New York City, 1909; on the staff of the Jewish Hospital; died Aug. 23, aged 73.

Breuer, Robert Eugene Ⓜ Rolla, Mo.; St. Louis University School of Medicine, 1907; member of the American Academy of General Practice; for many years member of the Phelps County Highway Commission; past-vice-president of the Missouri State Medical Association; for many years a member of the school board of Newburg; first chief of staff at the Phelps County Memorial Hospital, where he died Aug. 19, aged 77.

Broman, Martin Robert Ⓜ Evanston, Ill.; Rush Medical College, Chicago, 1916; certified by the National Board of Medical Examiners; fellow of the American College of Surgeons; veteran of World War I; in 1957 retired as pathologist at the Swedish Covenant Hospital in Chicago; died in Evanston Hospital Aug. 16, aged 66.

Bryant, J. Trevor Ⓜ Seattle; University of Oregon Medical School, Portland, 1940; interned at the French Hospital in San Francisco; certified by the National Board of Medical Examiners; associated with the Seattle General Hospital; died in the Swedish Hospital Aug. 26, aged 46.

Byers, Guy Ewing Gilfillan Ⓜ Salem, Ohio; Western Reserve University School of Medicine, Cleveland, 1918; served a term on the city board of health; past-president of the Columbiana County Public Health League; on the staff of the Salem City Hospital; past-president of the Salem Rotary Club; died Aug. 21, aged 67.

Caldwell, Hugh McIntyre Ⓜ Columbus, Wis.; Rush Medical College, Chicago, 1924; on the staff of St. Mary's Hospital; died in August, aged 59.

Carey, Michael Joseph, Council Bluffs, Iowa; St. Louis University School of Medicine, 1926; for many years on the faculty of Creighton University School of Medicine in Omaha; associated with the Veterans Administration Center in Des Moines; died in St. Joseph's Hospital in Omaha June 12, aged 62.

Cassidy, Patrick Homer, Salinas, Calif.; University of Washington School of Medicine, Seattle, 1958; interned at the University of Kansas Medical Center in Kansas City, Kan.; resident physician at the Monterey County Hospital; died Aug. 2, aged 36.

Chunn, Barker Daniel Ⓜ Beaumont, Texas; University of Texas School of Medicine, Galveston, 1934; interned at St. Therese Hospital; associated with Baptist Hospital of Southeast Texas, Hotel Dieu Hospital, and St. Therese Hospital; died Aug. 8, aged 52.

Clark, John Neal Ⓜ Vallejo, Calif.; University of California School of Medicine, San Francisco, 1941; interned at St. Mary's Hospital, where he served a residency; served a residency at the Solano County Hospital in Fairfield; member of the American Academy of General Practice; assistant health officer of Solano County; died Aug. 16, aged 47.

Coppridge, William Maurice Ⓜ Durham, N. C.; born in Danville, Va., July 24, 1893; Jefferson Medical College of Philadelphia, 1918; president of the American Urological Association and past-president of the Southeastern Section; specialist certified by the American Board of Urology; fellow of the American College of Surgeons; past-president of the North Carolina Urological Association, Medical Society of State of North Carolina, and the Durham–Orange Counties Medical Society; served as a member of the state board of medical examiners; for many years clinical professor of surgery at the University of North Carolina School of Medicine, Chapel Hill; formerly a member of the commission to study needs of medical education in North Carolina; veteran of World War I; a member of the North Carolina Committee for Procurement and Assignment of Physicians in Armed Forces during World War II; a member the county board of health; served as director of the laboratory of urology and chief of urology staff at Watts Hospital; died in the New England Baptist Hospital, Boston, Aug. 28, aged 66.,

Craig, Marion Stark Ⓜ Batesville, Ark.; Vanderbilt University School of Medicine, Nashville, Tenn., 1911; for many years owned and operated the Craig Hospital; a director of the Batesville Federal Savings and Loan Association; died Aug. 20, aged 74.

Degenring, Anna J., Elizabeth, N. J.; Woman's Medical College of Pennsylvania, Philadelphia, 1904; for many years a medical missionary in India; died in Springfield Aug. 28, aged 86.

Dix, George Alfred Ⓜ Worcester, Mass.; Harvard Medical School, Boston, 1899; veteran of World War I; served on the staff of the Worcester City Hospital; consultant on the medical board of the Memorial Hospital, where he died Aug. 20, aged 87.

Donald, Dan Caldwell Ⓜ Birmingham, Ala.; Tulane University School of Medicine, New Orleans, 1911; fellow of the American College of Surgeons; clinical professor of surgery at the Medical College of Alabama; past-president of the Jefferson County Medical Society; associated with Birmingham Baptist Hospital and the University Hospital; past-president of the Society of Medical History; died Aug. 21, aged 71.

Dozier, Byron T., Dallas, Texas; Barnes Medical College, St. Louis, 1897; died Aug. 19, aged 84.

DuVall, William Nelson Ⓜ Mishawaka, Ind.; Georgia College of Eclectic Medicine and Surgery, Atlanta, 1900; Bennett College of Eclectic Medicine and Surgery, Chicago, 1901; associated with St. Joseph's Hospital, where he died Aug. 20, aged 85.

Ehrlich, Ralph Louis, St. Louis; Washington University School of Medicine, St. Louis, 1925; formerly on the staff of the Robert Koch Hospital in Koch; on the staff of St. Anthony's Hospital; died in Maplewood Aug. 23, aged 59.

Evans, Claude Monroe, Marshall, Ark.; St. Louis University School of Medicine, 1909; died Aug. 13, aged 78.

Fama, Charles Ⓜ New York City; New York Homeopathic Medical College and Hospital, New York City, 1914; an honorary surgeon of the New York Police Department; served on the U. S. Board of Pension Surgeons and as a member of the medical board of the New York City Employees Retirement System; on the staff of the Union Hospital; died Aug. 29, aged 70.

Ferrell, George Stone Ⓜ Lynchburg, Va.; Medical College of Virginia, Richmond, 1940; veteran of World War II; interned at the Norwalk (Conn.) General Hospital and the Memorial Hospital in Wilmington, Del.; served a residency at the Sibley Memorial Hospital in Washington, D. C., St. Mary's Hospital in Grand Rapids, Mich., and the Riverside Hospital in Newport News, Va.; staff member of the State Hospital at Morganton, N. C., where he died Aug. 28, aged 46.

Frazier, Frederick Gary Ⓜ Chicago; Meharry Medical College, Nashville, Tenn., 1915; veteran of World War I; died in the Veterans Administration Hospital in Hines, Ill., Aug. 26, aged 71.

Frothingham, Channing, Boston; born in Brooklyn May 10, 1881; Harvard Medical School, Boston, 1906; past-president of the Massachusetts Medical Society; member of the Association of American Physicians; veteran of World War I; served on the faculty of his alma mater; overseer at Harvard College from 1936 to 1942; specialist certified by the American Board of Internal Medicine; trustee, Boston Psychopathic Hospital; consulting physician at the Eastern Maine General Hospital in Bangor, Maine, and the Faulkner Hospital; emeritus consulting physician at the Peter Bent Brigham Hospital; chairman of the Committee of Physicians for Improvement of Medical Care, Inc., from 1941 to 1947; chairman of the Committee for the Nation's Health; died in the Massachusetts General Hospital Aug. 11, aged 78.

Fuqua, Harold Boyd Ⓜ Terre Haute, Ind.; University of Illinois College of Medicine, Chicago, 1939; interned at the U. S. Marine Hospital in New Orleans; veteran of World War II and the Korean War; on the staff of the Union Hospital; died Aug. 13, aged 50.

Gardner, Leo Lloyd, Coral Gables, Fla.; Baltimore Medical College, 1907; formerly practiced in Chicago; died in the Jackson Memorial Hospital in Miami Aug. 18, aged 76.

Germain, Rodolphe T., Spokane, Wash.; University of Montreal Faculty of Medicine, Montreal, Que., Canada, 1896; died Aug. 15, aged 84.

Gilden, A. Morris Ⓜ Buffalo, N. Y.; University of Buffalo School of Medicine, 1920; associated with the Buffalo General Hospital; died in Hamilton, Ont., Canada, Aug. 16, aged 65.

Glass, Earl Floyd Ⓜ Wheeling, W. Va.; College of Physicians and Surgeons, Baltimore, 1907; associated with the Wheeling and Ohio Valley General hospitals; died Aug. 15, aged 80.

Gooder, William Verner Ⓜ Marengo, Ill.; Northwestern University Medical School, Chicago, 1905; veteran of World War I; died in Chicago Aug. 10, aged 78.

Gregg, Orion Russell Ⓜ Norman, Okla.; Kansas City (Mo.) Hahnemann Medical College, 1908; veteran of World War I; died Aug. 21, aged 74.

Grivelis, Evangel Ⓜ Brooklyn; University and Bellevue Hospital Medical College, New York City, 1931; associated with St. John's Episcopal Hospital; died Aug. 19, aged 68.

Hahn, Theodore F., De Land, Fla.; Baltimore Medical College, 1902; for many years a Presbyterian minister; a retired medical missionary; died in the Fish Memorial Hospital Aug. 20, aged 82.

Hamlin, Roscoe Earl, Santa Rosa, Calif.; College of Physicians and Surgeons of San Francisco, 1907; died Aug. 12, aged 80.

Harding, Samuel Asberry, Mocksville, N. C.; North Carolina Medical College, Charlotte, 1910; died in the North Carolina Baptist Hospital, Winston-Salem, Aug. 22, aged 71.

Hayman, Philip Paul Ⓜ Teaneck, N. J.; College of Physicians and Surgeons, Baltimore, 1911; died July 6, aged 71.

Hemminger, Edward F. Ⓜ Upper Darby, Pa.; Jefferson Medical College of Philadelphia, 1908; specialist certified by the American Board of Otolaryngology; on the draft board during World War II; served on the faculty of his alma mater; during his career served on the staffs of the Jefferson Hospital in Philadelphia, Bryn Mawr (Pa.) Hospital, and the Veterans Administration Hospital in Coatesville; died in the Delaware County Hospital in Drexel Hill Aug. 27, aged 76.

Hinshaw, Jonathan Dixon Ⓜ Canon City, Colo.; Kansas City (Mo.) Medical College, 1903; served as mayor; died Aug. 19, aged 85.

Hitchcock, Ethel Olivia Hunter, New York City; Cornell University Medical College, New York City, 1902; died May 22.

Holtzmuller, Charles William Ⓜ Farmersville, Ohio; Eclectic Medical Institute, Cincinnati, 1899; for many years president of the Citizens Bank of Farmersville; died Aug. 13, aged 85.

Jameson, Curtiss Norton Ⓜ Rochester, N. Y.; Rush Medical College, Chicago, 1902; veteran of World War I; associated with the Genesee and Rochester General hospitals; member of the American Society of Anesthesiologists, Inc.; died Aug. 22, aged 82.

Johnen, Arthur, West Norwalk, Conn.; Eclectic Medical College of the City of New York, 1897; died in the Norwalk (Conn.) Hospital Aug. 11, aged 98.

Kirkland, Luman Wilbur Ⓜ Beeville, Texas; Medical College of Alabama, Mobile, 1904; for many years county health officer; member of the American Trudeau Society; associated with the Beeville Hospital and the Thompson Memorial Hospital; on the board of directors of the Texas Tuberculosis Association; died Aug. 20, aged 77.

McClellan, Henry Joseph, St. Petersburg, Fla.; Baltimore University School of Medicine, 1898; died Aug. 10, aged 92.

Mahood, William Richmond, Santa Barbara, Calif.; University of Toronto Faculty of Medicine, Toronto, Ont., Canada, 1903; formerly practiced in Sioux City, Iowa; served on the staff of the Santa Monica (Calif.) Hospital; died Aug. 24, aged 83.

Marshall, Ernest Jones, Kansas City, Mo.; Northwestern University Medical School, Chicago, 1927; associated with the Wheatley–Provident Hospital and the Kansas City General Hospital; died Aug. 21, aged 74.

Martin, Clement Leon Ⓜ Chicago; born in Omaha March 9, 1891; Creighton University School of Medicine, Omaha, 1916; formerly a fellow in surgery at the Mayo Clinic, Rochester, Minn., where he was associate in the department of proctology; assistant professor of applied anatomy at his alma mater and on the surgical staff of St. Joseph's Hospital in Omaha from 1923 to 1926; clinical professor of proctology at Loyola University School of Medicine from 1927 to 1957; from 1948 to 1952 trustee of the Chicago Medical Society and past-president of the North Shore Branch; fellow, and in 1938-1939 vice-president of the American Proctologic Society; member of the International Board of Trustees, International College of Surgeons since 1952, since 1956 treasurer, and regent for Illinois of the U. S. Chapter, 1952-1953; fellow of the American College of Surgeons; member of the Institute of Medicine of Chicago and the Association of Military Surgeons of the United States; specialist certified by the American Board of Surgery; founder member, American Board of Proctology; director of proctologic division, Loyola–Mercy Clinics from 1939 to 1957; for many years consulting proctologist, City of Chicago Municipal Tuberculosis Sanitarium, Veterans Administration Hospital in Hines, Ill., Columbus Hospital, Oak Park (Ill.) Hospital, St. Bernard's Hospital, Alexian Brothers Hospital, and the Veterans Regional Office; senior attending proctologist, Mercy Hospital; died in the Presbyterian–St. Luke's Hospital Aug. 15, aged 68.

Mazur, Herbert Arthur Ⓜ St. Louis; Washington University School of Medicine, St. Louis, 1943; interned at Jewish Hospital in St. Louis; served a residency at St. Louis County Hospital in Clayton, Mo., and St. Louis Children's Hospital; instructor of clinical pediatrics at his alma mater; veteran of World War II; member of the American Academy of Pediatrics; specialist certified by the American Board of Pediatrics; staff member of Barnes and Children's hospitals and Jewish Hospital, where he died Aug. 23, aged 40.

Miller, George Louis, San Diego, Calif.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1902; died Aug. 12, aged 82.

Morell, Charles Joseph Ⓜ Philadelphia; Medico-Chirurgical College of Philadelphia, 1907; also a graduate in pharmacy; died in the Graduate Hospital of the University of Pennsylvania Aug. 26, aged 83.

Morgan, Harry Price, Wood River, Ill.; Bennett College of Eclectic Medicine and Surgery, Chicago, 1906; associated with the Wood River Township Hospital, where he died Aug. 14, aged 78.

Morrison, Winfield Scott Ⓜ Minonk, Ill.; the Hahnemann Medical College and Hospital, Chicago, 1905; for many years secretary of the Woodford County Medical Society; formerly county coroner; served as secretary of the board of education and the Woodford County Tuberculosis Association; for many years local surgeon of the Illinois Central Railroad; member of the Chamber of Commerce; in 1955 the Minonk Community honored him with "Dr. Morrison's Day" on July 4; associated with St. Mary's Hospital in Streator; died near Dana Aug. 17, aged 78.

Munger, Irvia Clarence Sr. Ⓜ Lincoln, Neb.; Illinois Medical College, Chicago, 1900; veteran of World War I; fellow of the American College of Surgeons; died Aug. 13, aged 84.

Munson, Leonard W., Milford, Conn.; Georgetown University School of Medicine, Washington, D. C., 1896; served on the staff of the Stamford (Conn.) Hospital; formerly medical examiner for Metropolitan Life Insurance Company; died Aug. 8, aged 90.

Nelson, Bendet, New York City; University of St. Vladimira Faculty of Medicine, Kiev, Russia, 1897; died June 19, aged 91.

Niedermeyer, Frederick Pierce Ⓜ Kansas City, Mo.; Northwestern University Medical School, Chicago, 1948; interned at St. Joseph's Hospital, where he served a residency; member of the American Academy of General Practice; veteran of World War II; served as a major in the U. S. Air Force Reserve; died Aug. 12, aged 36.

Opre, Harry E., Miami, Fla.; Chicago College of Medicine and Surgery, 1908; veteran of the Spanish-American War; died Aug. 9, aged 80.

Pamment, Harry Gill Ⓜ Toledo, Ohio; Rush Medical College, Chicago, 1913; served for 25 years as part-time epidemiologist for the city of Toledo health department; died Aug. 17, aged 74.

Patterson, Charles Henry, Lynchburg, Va.; University of Pennsylvania School of Medicine, Philadelphia, 1930; member of the American Academy of Dermatology and Syphilology; veteran of World War II; associated with the Lynchburg Training School and Hospital in Colony, and Virginia Baptist and Lynchburg General hospitals; died Aug. 9, aged 54.

Pavlidis, Isaac Michael, Havertown, Pa.; American University of Beirut School of Medicine, Syria, 1908; died in the Bryn Mawr (Pa.) Hospital Aug. 16, aged 82.

Pearce, Louise, Bell Mead, N. J.; born in Winchester, Mass., March 5, 1885; Johns Hopkins University School of Medicine, Baltimore, 1912; in 1941 appointed a member of the board of corporators, and from 1946 to 1951 president of the Woman's Medical College of Pennsylvania, where in 1952 she received a citation; received the Order of the Crown of Belgium for conducting the African sleeping sickness mission in the Belgian Congo in 1920-1921, sponsored by the Rockefeller Institute, with which she was associated for many years; visiting professor of syphilology at the Peiping Union Medical College in Peiping, China, 1931-1932; for many years a member of the general advisory council of the American Social Hygiene Association; member of the American Association of Pathologists and Bacteriologists and the American Society for Experimental Pathology; a trustee of the New York Infirmary, which in 1951 honored her with the Elizabeth Blackwell citation for achievement in medicine; from 1940 to 1946 a member of the board of Princeton (N. J.) Hospital; held honorary degrees from Wilson College, Bucknell University, Skidmore College, and the Woman's Medical College; died in the New York Hospital Aug. 10, aged 74.

Pearl, Nathaniel Ⓜ Long Beach, N. Y.; L. R. F. P. & S., of Glasgow, 1938; L. R. C. P., of Edinburgh, and L. R. C. S., of Edinburgh, Scotland, 1939; member of the American Academy of General Practice; veteran of World War II; associated with the Long Beach Memorial Hospital; died Aug. 6, aged 52.

Peete, Charles Henry Sr. Ⓜ Warrenton, N. C.; University of Virginia Department of Medicine, Charlottesville, 1903; served on the selective service boards during World Wars I and II; died Aug. 19, aged 80.

Person, Reuben Edward, Ola, Ark.; (licensed in Arkansas in 1903); died in St. Mary's Hospital, Russellville July 10, aged 78.

Pipes, David McKowen Ⓜ Baton Rouge, La.; Tulane University School of Medicine, New Orleans, 1934; member of the American College of Allergists; associated with the Baton Rouge Hospital and Our Lady of the Lake Hospital; died Aug. 25, aged 54.

Prunskis, Vladas, Chicago; Vytauto Didziojo Universiteto Medicinos Fakulteto, Kaunas, Lithuania, 1941; interned at the St. Elizabeth Hospital, where he was a member of the staff; died in the Albert Merritt Billings Hospital Aug. 21, aged 46.

Ransom, Harry Ensign Ⓜ Des Moines, Iowa; born in Avalon, Wis., Oct. 16, 1885; Marquette University School of Medicine, Milwaukee, 1914; city health commissioner from 1932 to 1951; assistant health officer from 1922 to 1932; served as secretary of the Polk County Medical Society, which in 1952 presented a bronze plaque in his honor to the city of Des Moines in recognition of his thirty years of efficient effort in establishing a modern health service for the city of Des Moines and surrounding community; veteran of World War I; associated with the Broadlawns Polk County Hospital, Iowa Lutheran Hospital, Mercy Hospital, and the Iowa Methodist Hospital, where he died Aug. 10, aged 73.

Reingold, Alexander, North Bergen, N. J.; University and Bellevue Hospital Medical College, New York City, 1914; for many years practiced in Hoboken; veteran of World War I; died Aug. 24, aged 67.

Renard, Suzanne Gesmar, New York City; Université de Paris Faculté de Médecine, France, 1922; made a Chevalier of the French Legion of Honor for nursing duties among French troops during World War I; died in Geneva, Switzerland Aug. 3, aged 71.

Rigby, Samuel B., Fairview, Utah; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; served four terms as mayor and five terms as Sanpete County commissioner; associated with Sanpete Latter-Day Saints Hospital in Mount Pleasant; died Aug. 7, aged 71.

Rosove, Leon Ⓜ Los Angeles; University of California School of Medicine, San Francisco, 1931; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World War II; associate clinical professor of medicine, University of California at Los Angeles School of Medicine; associated with the Los Angeles County Hospital and the Veterans Administration Center; died Aug. 11, aged 53.

Rudell, Gustave Leander Ⓜ Minneapolis; University of Minnesota Medical School, Minneapolis, 1906; veteran of World War I; died Aug. 8, aged 83.

Sayre, Philip Preston Ⓜ Onsted, Mich.; University of Michigan Homeopathic Medical School, Ann Arbor, 1914; past-president of the Lenawee County Medical Society and the Van Buren County Medical Society; associated with the Emma L. Bixby Hospital, Adrian, where he died Aug. 13, aged 73.

Scales, Emmet Thomas Ⓜ Des Moines, Iowa; State University of Iowa College of Medicine, Iowa City, 1927; member of the Endocrine Society and the American Academy of General Practice; at various times on the staffs of the Mercy, Broadlawns, and Iowa Lutheran hospitals; died Aug. 10, aged 58.

Shook, Ralph William Ⓜ Kalamazoo, Mich.; University of Michigan Medical School, Ann Arbor, 1927; for many years councilor of the Michigan State Medical Society; past-president of the Kalamazoo Academy of Medicine; served as lieutenant colonel in the Army Medical Corps in England during World War II; died in the James Decker Munson Hospital in Traverse City Aug. 9, aged 56.

Smith, Benjamin Averill Ⓜ Huntington, W. Va.; (licensed in West Virginia in 1897); died Aug. 11, aged 92.

Smith, Brainard Sutton Ⓜ Shaker Heights, Ohio; Harvard Medical School, Boston, 1954; interned at the New York Hospital in New York City; served a residency in pediatrics at the Cincinnati General Hospital and the Children's Hospital in Cincinnati; resident pediatrician at the Children's Hospital in Detroit; certified by the National Board of Medical Examiners; relieved as a captain in the medical corps of the U. S. Army Reserve in June, 1957; died in St. Luke's Hospital in Cleveland Aug. 22, aged 31.

Smith, Ellsworth Johnson, Madison, Conn.; Columbia University College of Physicians and Surgeons, New York City, 1904; veteran of World War I; formerly practiced in Larchmont, N. Y.; served on the staff of the New Rochelle (N. Y.) Hospital; member of the local health board; died Aug. 6, aged 80.

Sterns, Albert Henry Ⓜ New Bedford, Mass.; Tufts College Medical School, Boston, 1920; a member of the staff of St. Luke's Hospital, where he died Aug. 7, aged 65.

Stinchfield, Walter Scott Ⓜ Skowhegan, Maine; Bellevue Hospital Medical College, New York City, 1896; past-president and treasurer of the Maine Medico-Legal Society; for many years county medical examiner; died in the Redington Memorial Hospital Aug. 8, aged 86.

Stroud, William Daniel Ⓜ Philadelphia; born in Villanova, Pa., Nov. 20, 1891; University of Pennsylvania School of Medicine, Philadelphia, 1916; secretary of the Section on the Practice of Medicine of the American Medical Association from 1940 to 1944, when he became chairman, serving until 1946; specialist certified by the American Board of Internal Medicine; member of the Association of American Physicians, and the American Clinical and Climatological Association; fellow of the American College of Physicians, of which he served as treasurer; past-president of the American Heart Association and the Philadelphia Heart Association; assistant professor of clinical medicine at the University of Pennsylvania School of Medicine and professor of cardiology at the University of Pennsylvania Graduate School of Medicine; member of the board of directors of the Philadelphia Health Council and Tuberculosis Committee; veteran of World War I; chief of staff, Children's Heart Hospital; consulting cardiologist at the Abington (Pa.) Memorial Hospital, Norristown (Pa.) State Hospital, Bryn Mawr (Pa.) Hospital, St. Christopher's Hospital, and the Pennsylvania Hospital; editor of "The Diagnosis and Treatment of Cardiovascular Disease"; died in the Bryn Mawr (Pa.) Hospital Aug. 19, aged 67.

Sweet, Frank R., North Little Rock, Ark.; (licensed in Arkansas in 1903); died Aug. 7, aged 82.

Thomas, William Nelson Ⓢ Oxford, N. C.; Medical College of Virginia, Richmond, 1911; county health officer; for a long period county coroner; a member of the board of City Commissioners, Oxford Board of Graded School Trustees and Oxford Fire Department of which he was formerly chief; a director of Union National Bank, Oxford Building and Loan Association, and a charter member of the Oxford Rotary Club; associated with the Granville Hospital, where he died Aug. 3, aged 71.

Thompson, George Letcher Ⓢ Owensboro, Ky.; University of Louisville Medical Department, 1907; served as health officer of Owensboro, and McLean and Daviess counties; veteran of World War I; on the courtesy staff of the Owensboro-Daviess County Hospital, where he died Aug. 10, aged 81.

Trumpeter, John Horace Ⓢ Beaver, Pa.; University of Pittsburgh School of Medicine, 1922; specialist certified by the American Board of Obstetrics and Gynecology; past-president of the Beaver County Medical Society; formerly on the faculty of his alma mater; associated with the Beaver Valley General Hospital in New Brighton, Providence Hospital, Beaver Falls, and the Rochester (Pa.) General Hospital, where he died Aug. 9, aged 62.

Tyrrell, George Washington Ⓢ Perth Amboy, N. J.; College of Physicians and Surgeons, Baltimore, 1893; associated with the Perth Amboy Hospital; died in Keyport July 1, aged 89.

Uthoff, Carl Woodrow Ⓢ Grand Rapids, Mich.; Western Reserve University School of Medicine, Cleveland, 1943; interned at the University Hospital in Cleveland; served a residency at the Mercy Hospital in Toledo, Ohio; veteran of World War II; on the staff of the Butterworth Hospital; died Aug. 17, aged 42.

Vander Veer, Adrian Holt Ⓢ Chicago; born in New York City Nov. 4, 1909; Columbia University College of Physicians and Surgeons, New York City, 1934; interned at the Bellevue Hospital in New York City; served a residency at the Michael Reese Hospital; specialist certified by the American Board of Psychiatry and Neurology, Inc.; certified by the National Board of Medical Examiners; member of the American Psychoanalytic Association and the American Psychiatric Association; past-president of the Chicago Council of Child Psychiatry; at one time on the faculty of Rush Medical College and the University of Chicago, The School of Medicine; served on the staff of the Cook County Psychopathic Hospital; died in the Michael Reese Hospital Aug. 13, aged 49.

Warrick, Will Carleton, Pontiac, Mich.; University of Illinois College of Medicine, Chicago, 1914; served on the staff of the Pontiac General Hospital, where he died July 25, aged 71.

Waters, Chester Thomas, Dallas, Texas; Louisville (Ky.) and Hospital Medical College, 1908; for many years associated with the Veterans Administration; died Aug. 11, aged 71.

Watts, Wilbur Ⓢ Trenton, N. J.; University of Pennsylvania Department of Medicine, Philadelphia, 1907; specialist certified by the American Board of Otolaryngology; veteran of World War I; associated with St. Francis Hospital, where he served as president of the staff and chief of otolaryngology; died Aug. 12, aged 75.

Webb, Jonathan Warner, Parkersburg, W. Va.; Baltimore University School of Medicine, 1905; died July 22, aged 82.

Welch, Robert Sellman Gray Ⓢ Annapolis, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; past-president of the Anne Arundel County Medical Society; fellow of the American Academy of Ophthalmology and Otolaryngology; served in the regular U. S. Navy; veteran of World War I; for years served as chairman of the Anne Arundel Welfare Board; associated with the Anne Arundel General Hospital, where he died Aug. 5, aged 66.

Welch, Winthrop Sherwood Ⓢ Torrington, Conn.; Cornell University Medical College, New York City, 1941; interned at the Hartford (Conn.) Hospital, where he served a residency; medical officer in a combat infantry unit in the Pacific Theater during World War II; associated with the Charlotte Hungerford Hospital; died July 20, aged 46.

Wentworth, Daniel Webster, St. Petersburg, Fla.; Medical School of Maine, Portland, 1899; veteran of World War I; died in Eliot, N. H., July 29, aged 89.

Williams, Harold Otis Ⓢ Kendallville, Ind.; Indiana University School of Medicine, Indianapolis, 1913; member of the American Academy of General Practice; past-president of the Twelfth District of the Indiana State Medical Association and the Noble County Medical Society; for many years member of the city council; veteran of World War I; surgeon for the New York Central and Pennsylvania railroads; physician for the police department; associated with the McCray Memorial Hospital, where he died Aug. 1, aged 69.

Wilson, James Cathcart, Holly Hill, Fla.; Columbia University College of Physicians and Surgeons, New York City, 1922; served on the staff of the Lawrence Hospital in Bronxville, N. Y.; died in the Halifax District Hospital, Daytona Beach, Aug. 23, aged 61.

Wolfson, Isaac Edward Ⓢ Los Angeles; University of Cincinnati College of Medicine, 1931; veteran of World War II; died in the Cedars of Lebanon Hospital July 20, aged 54.

FOREIGN LETTERS

BELGIUM

Roentgenography of the Prostate.—Roentgenographic studies of the prostate are still rarely made. Blum and Sichel (*Acta urologica belgica*) described a new technique for such studies. Tomograms of the prostate are made after filling the bladder with 100 to 150 cc. of air, oxygen, or carbon dioxide. Because of the simplicity and safety of this method it should become the method of choice. It provides information about the size and form of adenomas not easily perceptible on rectal examination and helps to establish precise diagnosis of epithelioma of the prostate by exactly determining the degree of endocystic invasion. In case of a prostatic abscess tomography shows unsuspected aspects of deviation of the affected lobe and compression of the nonaffected lobe.

Detection of Alcoholic Intoxication.—In detecting alcoholic intoxication, particularly that involving automobile accidents, there has been a tendency for some time to estimate the level of alcohol in the blood by analysis of the expired air. Moreau and co-workers reported at the Academie de Médecine that the method of Schuhe and Frey deserves to be looked on as a preliminary test by which alcoholic intoxication may be excluded, thus making blood tests unnecessary if the suspicion is confirmed. Comparing the results of this test with those obtained by blood analysis has shown, however, that there are great variations depending on whether the subject breathes merely until a certain signal lamp has been lighted as recommended or with maximum expiration. In the latter case the chances that the automatic dosage will affect the alveolar air rather than the bronchial air are increased and the agreement with the blood level becomes better as a result. Reliance on an analysis of the expired air is therefore not justifiable.

Atypical Myocardial Infarction.—Ghys (*Acta cardiologica*) reported a series of 248 patients with myocardial infarction. The physician should know that among the patients with myocardial infarction 5 to 10% are atypical in that no pain is associated with the lesion. The absence of pain in those patients can be explained either by the destruction of the sensory endings in the infarcted zone or by the impermeability of the synapses of the posterior horn of the spinal cord to cardiac stimuli. On the other hand, pain is manifested in an atypical localization in a fair percentage of the patients. There may be acute pain in the epigastrium associated with abdominal rigidity leading to unnecessary and even dangerous laparotomy. Apparent indications for an immediate operation should not interfere with obtaining an electrocardiogram in patients with symptoms suggestive of a perforated peptic ulcer. Furthermore a significant number of patients with myocardial infarction do not show pathognomonic electrocardiographic manifestations, because of either ventricular tachycardia or a disturbance in the atrioventricular conduction (bundle-branch block). It is important, therefore, to investigate carefully both subjective and objective signs of myocardial infarction in patients who suddenly present atrioventricular or interventricular heart block.

BRAZIL

Hibernotherapy for Eclampsia.—A series of 30 patients with eclampsia were given a lytic cocktail by Dr. Caetano Giordano and co-workers (*Revista de ginecologia e d'obstetricia*, July, 1959). Artificial hibernation had no statistical or clinical advantages over treatment with magnesium sulfate, as regards the disappearance of convulsive crises or maternal and fetal mortality, nor was it effective in combating hypertension.

Schistosomiasis.—Dr. J. Pelegrino and co-workers of the University of Minas Gerais (*Jornal de Pediatria*, May, 1959) compared the results obtained by stool examination with those obtained by intradermal tests using adult schistosome antigen and quantitative complement-fixation tests for the diagnosis of intestinal schistosomiasis. The observations were made on 234 unselected school children aged from 10 to 15 years and living in an endemic area near Belo Horizonte. Stool examination was repeated up to four times in those children presenting negative first stool examinations and positive or doubtful immunological tests. Rectal biopsy was performed on those with repeated negative stool examination. Positive results were obtained in 59.4% of the stool examinations, 42.7% of the intradermal tests on the forearm, 59% of the intradermal tests on the back, and 66.7% of the complement-fixation tests.

Clinical examination of 63 infected and 48 noninfected children showed the difficulties of clinical diagnosis of this disease. The authors suggested the following schedule for the diagnosis of intestinal schistosomiasis in children. In patients suspected clinically of having the disease stool ex-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

amination may be performed and, if negative, a complement-fixation test and skin test on the back should be made. If one of the immunological tests is positive, stool examination should be repeated up to four times and if still negative rectal biopsy should be performed. In epidemiological surveys complement-fixation tests and stool examinations give equally satisfactory results, but the complement-fixation test has certain practical advantages. The results of the skin tests in epidemiological surveys should be interpreted with caution.

CANADA

Canada's Health.—At the joint meeting of the British and Canadian Medical Associations Dr. Gordon Wride (Ottawa) gave an account of the Canadian national sickness survey. At the time of the survey each person had in one year approximately one disability period due to illness, lasting on an average 12 days. Of those suffering from illness 75% did not stop their usual activities. Days confined to bed averaged 5.6 per person.

Over 75% of those reporting sickness had new illnesses during the survey period, the incidence being highest in children. The highest incidence of illness occurred in those under 15 years of age, and the lowest in those aged 15 to 24. After this age the period of sickness tended to increase steadily with age. Women had slightly more illness than men (60.7% of all women compared with 56.2% of all men), and 52% of all women required some period of treatment in bed, compared with 44.1% of men. These differences could be partly explained by the incapacity of young adult women in the childbearing age. The common cold and influenza caused more absenteeism than all other illnesses. After these were gastric complaints, acute pharyngitis, and conditions with symptoms in the back and limbs. Respiratory disease was common in children, more than 75% being affected in the survey period. After this in order of frequency were infective and parasitic diseases.

The diseases affecting the group aged 45 to 65 years were mainly those affecting the bones, limbs, and circulatory system. The survey showed that 80% of the population had some illness in the course of a year and that in this time each person affected has an average of 2.5 bouts of illness. Just over 50% of the population reported some medical care by physicians. Of this 43% was given by general practitioners, and 10% of all patients had inpatient treatment. More than 40% of the population received calls from physicians or made office visits. The physician was consulted in 25% of all cases of illness. House calls were made mainly for those under 15 and those over 65 years of age. The average number of physicians' calls or visits per 1,000 population was 1,786 or 1.8 per person per year. The average number of days per person spent in the hospital increased with age.

The 4,555,000 family units making up Canada's population spent $373,800,000 on health services in the survey period. Direct payment to physicians was made by 23.5% of the population and indirect payment through prepayment plans by 3.2%. The survey revealed that one million Canadians have a permanent disability of some sort; 414,000 are severely disabled; and 90,000 "totally" disabled, but 33% of the "totally" disabled are at work. In order of frequency the disabilities were due to heart and arterial disease, accidents, arthritis and rheumatism, disorders of the nervous system, deafness, and blindness.

FINLAND

Deaths from Parathion.—Parathion, first used as an insecticide in World War II, is now being used in increasing quantities. Due to its anticholinesterase action and the resulting rise in acetylcholine concentration it stimulates the parasympathetic nervous system and peripheral nerve endings. Exposure to high concentrations, which may enter the body through the respiratory tract or skin, can cause death within a few minutes, although the usual period is one-half-to-four hours. Toivonen and coworkers in Helsinki reported the increasing frequency of parathion poisoning (*Lancet* 2:175, 1959). Between 1952 and 1957 there were 286 deaths in this country due to parathion pesticides. In the last year for which figures are available there were 105 deaths. Of the total number of deaths only 17% were accidental, the remainder being suicidal. The number of suicides in Finland from taking parathion is greater than that from hypnotics and barbiturates. The latter are responsible for about 40% of the total number of suicides. Most of the accidental deaths were in small children given a parathion mixture in mistake for medicines, such as cough mixtures. In adult accidents a parathion mixture was frequently taken inadvertently in a period of alcoholic intoxication. In 20% of the deaths the victim had access to parathion in the course of his or her work. The remaining 80% seem to have had little difficulty in buying or acquiring the poison.

FRANCE

Ureteral Calculi.—J. and E. Thomas and co-workers at the meeting of the National Academy of Medicine on April 7 reported that neither a solution of lithium salts nor a solution of urea were found to be capable of dissolving uric acid calculi in situ. On the other hand, a solution of piperazine did dissolve such calculi. Since piperazine is a strong base it is necessary to bring the pH of this solution to 8 or 9 when it is used for urologic purposes. This can be accomplished by adding phosphoric acid. Under these conditions a solution of piperazine containing 17.8 Gm. per liter dissolved 5 Gm. of uric acid per liter at a temperature of 20 C. To avoid disturbances connected with resorption a solution of piperazine of 5 Gm. per liter was recommended. This was given by intraureteral perfusion for a few hours daily. Too long a perfusion period may result in an undesirable piperazine resorption.

Cigarette Filters.—At the meeting of the same Academy on May 12, J. Paraf and co-workers reported on the use of a filter which they perfected. It consists of cotton impregnated with polymerized furfural. The study was made in heavy smokers who had no organic lesions in the respiratory tract. A series of 76 persons smoked cigarettes with common commercial filters, and 61 smoked with furfuralized cotton filters. In the first group the undesirable respiratory and other side-effects were reduced by about 22% of the intensity observed when cigarettes with no filters were smoked, but in those who used furfural filters the average reduction was 50%. Here it must be added that in 25% of the subjects side-effects were completely or almost completely eliminated. Laryngeal, tracheal, and bronchial irritation and nausea and anorexia disappeared. It is important that the smoker retain the taste of the smoke because when this is masked or weakened, the smoker inhales more vigorously and this diminishes the effectiveness of the filter. Also by increasing the temperature of the smoke passing through the filter the production of noxious elements is increased. The authors believed that no other filter so effectively retains tars and nicotine without diminishing the aromatic qualities of the smoke as does theirs.

Late Results of Operation for Gallstones.—At the meeting of the Academy of Surgery on May 20, B. Kourias and A. Tobler reported on a series of 550 patients who had been operated on for gallstones between 1950 and 1955. The results were excellent in 70.4% of the patients. There were no symptoms even in those who committed dietary excesses. In 17.4% mild symptoms occurred after dietary indiscretion. In 6.5% of the patients some improvement was observed but they still had occasional attacks of pain. Relapses or operative failures were noted in 5.7%. Operative failures were due to stones overlooked in the principal biliary passages, biliary dystonia, colitis, or hydronephrosis. The mild symptoms present in some were believed to be due to transient dystonia of the biliary duct because of ablation of the gallbladder, chronic pancreatitis, or hepatitis. The excellent results were attributed by the authors to the preoperative use of cholangiography.

Psychic Disturbances due to Isoniazid.—A. Lepeuple and co-workers (*Revue de Tuberculose et de Pneumonologie,* no. 3, 1959) studied a series of 621 tuberculous students of about the same age and mental level, who were treated with isoniazid. Such psychic disturbances as discreet hypomania, mania, manic-depressive psychosis, and confused dreamlike states are frequently produced by this drug. Previous psychic disturbances existed in 7% of the 621 students. Severe psychosis and neurosis was found in 4.6% of them. These factors must be taken into account in interpreting the disturbances occurring following the use of isoniazid. Thus, among the patients who had no history of psychic disorder, only 1.56% manifested such disturbances, as compared with the occurrence of these disorders in 33% of those who had had previous psychic disorders. On the other hand, the daily dose had no clearly defined influence on the occurrence of these disorders. The blood level of free isoniazid, which is not always in proportion to the absorbed dose, plays an important role. The patients who manifest psychic disorders with a low isoniazid level are those who were previously the most severely disturbed. It is possible that there is a threshold of toxicity in each person beyond which psychiatric complications may occur. This threshold is lower in persons with a history of previous psychic disorders.

Paralysis Agitans.—P. Morin (*Revue Médicale Normande,* no. 1, 1959) studied a series of 100 patients with paralysis agitans who were operated on by pallidolenticular coagulation. The operation was performed with the patient (previously subjected to trepanation) conscious and consisted of local electrocoagulation. The author observed two severe complications; one patient had a fatal hemorrhage and the other became confused, but he recovered completely within two months. In 75% of the patients the tremor and rigidity disappeared either immediately after electrocoagulation or within a few weeks. A certain number of patients had a mild relapse. This operation had, on the other hand, a variable effect on walking and on general motility. In some patients there was a marked improvement and in others none at all. Speech, facies, and hypersialorrhea were not improved and sometimes were aggravated. The best results were obtained in young patients whose disease was predominantly unilateral and of short duration.

Cobalt and Penicillin.—C. H. Chouard (*Revue de Pathologie Générale et de Physiologie Clinique,* 1959) emphasized the quantitative and qualitative increase in the effectiveness of penicillin when given with cobalt acetate. A series of 24 patients who had acute exudative otitis and other otolaryngologic infections was treated with this combination. The results were favorable in all. Three patients with acute exudative otitis were cured without paracentesis within two to six days. Six patients with otitis, in which the protracted course suggested mastoiditis and who were subjected to paracentesis, were completely cured within a fortnight. Of five patients with suppurative adenitis of the neck, three were cured without any other therapy. One patient with nasopharyngitis was cured within a few days. The condition of two patients with nasopharyngitis associated with otitis was improved within one week. Some authors believe that cobalt leads to a diminution of the oxygen consumption by the bacteria. Others suggest that cobalt increases phagocytosis. Cobalt works synergically with no other antibiotic than penicillin.

GERMANY

Resection of the Thoracic Section of Esophagus.—H. Manseck (*Zentralbl. Chir.* 83:301, 1958) stated that even when treatment of intrathoracic pressure made possible resection of the thoracic portion of the esophagus, this operation was justified only in patients with malignant tumors. Advances in surgery in the last 10 years have helped to reduce the danger in such an operation. These advances include the introduction of antibiotics, the management of pressure difference on opening the thorax, and perfection of a technique for using the stomach as a substitute for the esophagus. Potentiated curare narcosis, after use of high-pressure narcosis with intubation, has been of great value. The author reports on two patients on whom a transthoracic operation, without opening the abdomen, was performed. One patient had a resection of the cardia because of suspected malignancy with stenosis and the other had an epiphrenal diverticulum that had caused marked dilatation of the esophagus. Both patients were cured. Benign tumors of the esophagus usually do not require resection. They can be removed by endoscopy, like papillomas or mucosal polyps. Manseck avoids wide opening of the abdomen and thus greatly reduces the operative trauma.

Asbestosis.—Hertz and Reinwein (*Ärztl. Wchnschr.* 14:361, 1959) reported on three patients who had worked with asbestos insulation for 10, 21, and 23 years. They were admitted because of chronic bronchitis refractory to treatment. All had the subjective symptoms of pulmonary fibrosis: cough with tenacious sputum, stabbing and dull pains in the thorax, and dyspnea. The sputum in all three contained asbestos bodies, which could be demonstrated by adding to the sputum an equal amount of Antiformin (sodium hypochlorite), centrifuging, and examining the deposit microscopically. Typical radiologic changes of the lung consisting of strand-like shadows and cloudy turbidities in the lower lobes were present in only one patient. There is often a significant discrepancy in asbestosis between clinical and roentgenographic findings. Pulmonary changes demonstrable by radiology are usually much more unobtrusive than in silicosis. Asbestosis cannot, therefore, be diagnosed by x-ray examination alone, since this method reveals mainly alterations of the substrate, but not the primary functional disorders that constitute the first clinical symptoms.

Testing of pulmonary function showed that, according to the degree of pulmonary fibrosis present, vital capacity was reduced in all three patients as the result of a restrictive disturbance of ventilation. Expansion capacity of the lung was diminished due to increased rigidity of the tissue and, therefore, elastic resistance was increased. One patient had an obstructive ventilatory disturbance also. Disturbances of pulmonary function were generally greater than might be thought from the roentgenograms. Puncture for a sanguinolent pleural effusion was made in one patient. Although the effusion did not contain tumor cells, an asbestos carcinoma, which is found in about 20% of cases, was suspected. Asbestosis should be recognized as an occupational disease. Since management of the disease, as of all other pneumoconioses, is confined to purely symptomatic treatment, preventive measures are of great importance. If impairment of pulmonary function is already manifest, it is imperative to remove the patient from the hazardous surroundings in order not to aggravate the unfavorable prognosis of asbestosis by further exposure.

Penicillin-resistant Gonococci?—H. Röckl (*München, med. Wchnschr.* 101:708, 1959) stated that penicillin-resistant gonococci have not emerged after more than 10 years of treating gonorrhea with penicillin. The so-called penicillin failures are attributable to diagnostic mistakes (confusion with pseudogonococcic strains); reinfection; and insufficient penicillin dosage or local conditions preventing an adequate antibiotic level at the site of infection. The question whether the penicillin sensitivity of gonococcic strains has decreased in the course of the years was investigated by means of gonococcic cultures; 52 strains were tested in the first half of 1956, and 51 strains two and one-half years later. The strains were selected at random from patients with gonorrhea.

The collective mean of total growth inhibition was 0.0058 U. per milliliter in 1956 and 0.0150 U. per milliliter in 1958, which shows a marked increase. While a penicillin concentration of 0.01 U. per milliliter effected total inhibition in 57% of all strains in 1956, the corresponding figure for 1958 was only 23%. The highest limit of growth (0.1 U. per milliliter in 1956) was surpassed in 1958 by three collective strains. These results show a significant decline of penicillin sensitivity of gonococci, which is ascribed mainly to a gradual adjustment of gonococci to penicillin in the course of the years, besides the factor of selection (eradication of sensitive strains). Complete resistance has not, however, developed.

Cardiac Decompensation.—In cardiac therapy digoxin is of special importance. Because its action is intermediate between the fleeting action of strophanthin and the sustained retention of digitoxin, it offers great advantages in general practice. In combination with oxyethyltheophylline and nucleosides it affords a convenient means of treatment. P. Könner (*Medizinische* 11:469, 1959) used such a composite preparation, Parmanil-digoxin, to treat a series of 65 patients. The preparation was well tolerated and the author pointed out the improved glycoside tolerance, increased diuretic effect, and improvement of cerebral and coronary circulation resulting from its use. The latter property is important because cardiac decompensation is associated with coronary insufficiency in most patients. The drug is suited for the treatment of all types of cardiac insufficiency, including the specially glycoside-sensitive forms.

The guide for dosage is the pulse rate which usually returns to normal within five to seven days. In 50% of the patients treatment was initiated with intravenous injections, giving one ampul two times daily for about five days. Thereafter treatment was changed to tablets. The other group received the preparation orally from the start: 3 tablets daily were required until saturation was achieved in four or five days; for maintenance usually 2 tablets daily were required. The rapid onset of dehydration (diuresis) in most patients rendered additional diuretic medication superfluous and prevented the passage of glycoside into the congestion fluid, thus, precluding incalculable redigitalization.

Ionizing Radiation of Cutaneous Cancer.—C. G. Schirren of the University of Munich (*München. med. Wchnschr.* **101**:1269, 1959) evaluated various methods in the management of cutaneous cancer by means of ionizing radiation. These included contact irradiation; soft-ray irradiation by means of the beryllium tube; y-rays originating from the series of natural (radium) and artificial (cobalt) radioactive substances; beta-radiation with strontium, yttrium, and phosphorus; and the electron accelerator. Those methods are theoretically preferable which deliver the largest possible concentration of the dose to the tumor. From this standpoint the electron accelerator is the method of choice. Due to extremely high purchase and maintenance costs, however, it cannot be generally used. Apart from special cases, y-radiation produced no better therapeutic results than contact and soft-ray irradiation. Their application, however, is more complicated and is associated with a stronger genetic stress. Beta rays possess a limited range of indication, as they can be used only to treat flat tumors. Among the methods of ionizing radiation, radiotherapy is still of greatest significance for practice. In the therapy of cutaneous cancers soft radiation is now replacing contact radiation.

Death of Prof. Adolf Windaus.—According to a report in the *Deutsche medizinische Wochenschrift* of Aug. 21 Adolf Windaus, emeritus professor of chemistry and former director of the Chemical Laboratories of the University of Göttingen, Germany, died recently at 82 years of age. He was an outstanding biochemist who made important contributions, particularly to the study of vitamin D and its use in the prophylaxis and treatment of rickets. In 1928 the Nobel prize in chemistry was awarded to him for his studies on the nature of sterols and their connections with vitamins. Later studies in his laboratory contributed to the investigation of a chain of ergosterols, such as lumisterol, tachysterol, calciferol (vitamin D_2), activated 7-dihydrocholesterol (vitamin D_3), suprasterol, and dihydrotachysterol.

INDIA

Chlorpromazine for Tetanus Neonatorum.—Nazareth and Edibam (*Indian Journal of Child Health*, vol. 8, July, 1959) achieved a significant reduction in the mortality of tetanus neonatorum with the use of chlorpromazine. The usual treatment with sedatives, antibiotics, and antitetanic serum had resulted in a death rate of about 88%, but with a combination of chlorpromazine, antitetanic serum, and procaine penicillin this was reduced to 56%. The authors treated a series of 16 patients who had tetanus neonatorum with this combination. All of these infants were delivered at home by an unqualified midwife or a relative without any aseptic precautions. The age of the infants on admission was between 5 and 21 days. In 12 patients with an incubation period of seven days or less, only 4 survived. Of four with an incubation period of eight days or more, three survived. Survival in the patients with a short incubation period was attributed to the use of chlorpromazine. The period of onset is also important in the prognosis. There is a greater chance of survival when this period is longer than 24 hours. Of eight patients whose period of onset was less than 24 hours, only one survived but of the remaining eight with a longer period of onset six survived.

The first sign of the disease was failure to nurse. This was followed by stiffness of the back and spasms. The umbilicus was sodden or moist in all except one who had gross umbilical sepsis. A positive gag reflex was an important diagnostic sign, generalized spasms being induced by attempts to open the mouth. Eleven had severe and five had mild spasms. All in the latter group and only two in the former survived. Fever lasting for more than

48 hours after admission was a bad prognostic sign. Two infants who were afebrile throughout survived but another had severe spasms and died 40 hours after admission.

Treatment was carried out in a separate darkened room, feeding being left to nurses. Locally only simple dressings were used for the umbilicus. Treatment consisted of administration of procaine penicillin and aspirin. Tetracycline was given to three patients but was of no help. Prednisolone was given to two patients to control fever but was also of no help. For sedation, chlorpromazine was used in a total daily dosage of 14.3 mg. per kilogram of body weight. Excellent sedation was obtained in patients with moderately severe spasms. Of six such patients, only one died. Sedation lasted for one to two hours and the babies went to sleep about 20 minutes after injection. They could be aroused for a feeding and slept immediately afterward. Although spasms recurred in two hours, they were much reduced in frequency. In patients with severe spasms chlorpromazine alone did not help and secobarbital per rectum used in addition controlled the spasms for four or five hours. In seven patients spasms could not be controlled even with both of these drugs. These had had a short onset and all of them died. No toxic effects were observed with the use of chlorpromazine in this dosage. The injections could be given at six-or-eight-hour intervals and even slightly larger doses than those used here might be used to control the spasms more effectively. The drug was given till the baby started taking oral feedings. Usually it had to be given for about 10 days after admission.

The authors got better results with chlorpromazine in childhood tetanus than in tetanus neonatorum but even in the latter its use led to an increase in recovery rate. Tube feeding was started on admission and the tube could be passed more easily 15 to 30 minutes after injection of chlorpromazine. It was changed every 24 hours. Tube feeding, however, carries the risk of inhalation of regurgitated milk and three patients in this series died of this complication. Oral feedings could be started by about the seventh or eighth day. Subcutaneous infusion was used in only one patient and he died. The authors recommended avoidance of any infusions during the first eight days. No operations such as tracheotomy or umbilectomy were performed on any of the patients. The usual dose of antitetanic serum was 30,000 units. This comparatively small dose was found to have certain advantages. Thus, the initial temperature after the administration of the serum returned to normal much earlier and remained so. A secondary rise sometimes occurred on the fourth to seventh day but this was also mild. The smallness of the dose did not influence the cure rate adversely. The total quantity of serum injected being much less, there was less pain at the site of injection and the chances of abscess formation were also similarly reduced. Economically it is of great advantage.

Tranquilizers.—F. N. Shroff and co-workers (*Journal of J. J. Group of Hospitals and Grant Medical College*, vol. 4, July, 1959) assessed the tranquilizing effects of chlorpromazine, reserpine, meprobamate, and an indigenous drug known as malakanguni in an experimental study. In one group of experiments, the effect of these drugs on convulsions produced by epinephrine, pentylenetetrazole, picrotoxin, and strychnine was observed. The dose of the convulsant was such as to produce 100% mortality in 10 rats. Tranquilizers were injected either before or simultaneously with the LD_{100} of the convulsant drug. The behavior pattern of albino rats was studied after a single dose of these drugs and the sedative effect noted. Their effect on pentobarbital anesthesia was observed by first injecting the pentobarbital intraperitoneally in mice and noting the onset of sleep and righting reflex time. The drug to be tested was then given simultaneously or one hour before the barbiturate injection and alterations, if any were noted.

The antispasmodic effect of these drugs was studied on isolated guinea pig ileum and rabbit duodenum preparations. Contractions were induced with acetyl choline or histamine. The drugs to be tested were injected in the bath three minutes prior to injection of acetyl choline or histamine and the effect on contractions noticed. Of the convulsants used in rats, epinephrine caused marked excitement and 60% mortality in the dosage used, while with the other convulsants there was 100% mortality. None of the tranquilizers could counteract the effect of epinephrine. Meprobamate, chlorpromazine, and reserpine actually led to an increase in the mortality induced by this drug. Meprobamate was remarkably effective in convulsions induced by pentylenetetrazole, producing a 100% reduction in mortality. Malakanguni lowered the mortality by 60%. Chlorpromazine and reserpine had no effect on these convulsions. Meprobamate reduced the mortality after picrotoxin convulsions by 40%, reserpine by 100%, malakanguni by 20%, and chlorpromazine was ineffective.

This difference in action of the tranquilizers may be related to their different sites of action. Meprobamate antagonized strychnine completely while the other drugs did not show much effect. Malakanguni and reserpine actually enhanced the effects of strychnine. The righting reflex time was increased by reserpine, malakanguni, and chlorpromazine. All except meprobamate had a potentiating effect on the sedative action of pentobarbital. The reduction in mortality was not significant with any of the drugs. As an antispasmodic, meprobamate was ineffective, malakanguni caused 50% reduction, and chlorpromazine and reserpine showed some antispasmodic action. Meprobamate was unique in its action against strychnine, which was not shared by other tranquilizers. From the different effects observed, these drugs have been divided into autonomic suppressants and central relaxants. The relaxants would be primarily helpful in the treatment of psychoneuroses and the autonomic suppressants could be helpful for treatment of psychoses. The indigenous drug, malakanguni, was noted to have all the properties of a tranquilizer.

Hypertension.—M. J. Pandit studied the incidence of hypertension in 1,978 men and 1,267 women attending the J. J. Hospital, Bombay (*Journal of J. J. Group of Hospitals and Grant Medical College,* vol. 4, July, 1959). The patient was considered to be hypertensive if the basal reading (readings were taken at 5-minute intervals after the patient had been lying down for 15 to 20 minutes, till a constant reading was obtained), was persistently high (160 mm. Hg or over for the systolic and 100 mm. Hg or over for the diastolic pressure). In the author's series 65 patients were found to be hypertensive, giving an incidence of 2%. The incidence was slightly higher in women than in men. No positive family history of hypertension was obtained from any patient. Body build was determined in 30 hypertensive patients, 6 were stout, 19 average, and 5 thin. Most of these patients belonged to the poor working class and indulged in an active occupation. Psychological factors were probably partly responsible in 5 of the 30. Eight patients had secondary hypertension, five of renal origin, and all were below 40 years of age; the remaining 22 had primary hypertension and were 40 years of age or over. In 28 the hypertension was benign and in 2 it was malignant. Giddiness, dyspnea, and headache were the most common symptoms.

Venereal Diseases.—Tampi and Rao (*Indian J. Dermat. & Venereal.* 25:2 [April-June] 1959) analyzed the source of infection in 1,358 patients (1,248 men and 110 women) attending the venereal disease clinic between 1954 and 1959. Of these patients 227 were not sure about the source; 257 had primary syphilis, 207 secondary syphilis, 270 gonorrhea, and 624 chancroid. Of the women, 88 acquired the infection from their husbands, while 170 men got the infection from their wives. Of the remaining 873 for whom the source of infection was known, in 418 or 47.9% it was acquired from prostitutes.

Encephalitis in Children.—Manchanda and Gupta (*Indian Journal of Child Health,* vol. 8, July, 1959) studied 45 children who had a diagnosis of encephalitis in the summer of 1958. The criteria for diagnosis were an acute onset with fever, involvement of the central nervous system after a variable prodromal period, and drowsiness or coma. Convulsions, if present, were followed by unconsciousness usually for more than 24 hours. The spinal fluid showed bacteriologically negative findings and a normal or elevated cell count. These cases occurred between July and October. The youngest patient was 8 months old and the oldest was 11 years of age. In only five was there a history of similar disease in another member of the family or in the immediate neighborhood.

The clinical findings conformed to one of four types: (1) acute fulminating onset with vomiting, chills, and a temperature of 107 to 109 F; (2) acute infection with cerebral involvement, with rigidity, convulsions, and drowsiness or coma; (3) acute gastroenteritis with vomiting and diarrhea leading to severe dehydration and circulatory failure within 24 hours; and (4) insidious onset but after a variable period, with evidence of one of the above patterns. Treatment essentially consisted of hydration, resuscitation, hydrotherapy, sedation, and antibiotic therapy, the latter including parenterally administered crystalline penicillin, streptomycin, and broad-spectrum antibiotics. An acute onset with chills, gastrointestinal symptoms, high temperature, coma, and convulsions was associated with a bad prognosis. No form of treatment seemed to influence the prognosis. Follow-up revealed the presence of left-sided hemiplegia in two patients and mental changes in two. In this epidemic 26 patients died.

Dermatomycoses.—R. N. Gupta (*J. Indian M. A.* 33:2 [July 16] 1959) analyzed a series of 620 patients with dermatomycoses and found that Trichophyton rubrum was the most prevalent species responsible for this disease. T. rubrum caused 56.73%, T. mentagrophytes 31.73%, Epidermophyton floccosum 1.92%, and other organisms 9.62%. Although all parts of the body may be affected, the groins and genitals followed by hands, feet, face, scalp, and nails were most commonly involved, and the men outnumbered women 3:1. Adults accounted for 60.32% of the cases, persons 12 to 20 years old for 33.23%, and younger children for 6.45%.

UNITED KINGDOM

Nurses' Examinations.—In a letter to the *Lancet,* Drs. Walther and Raeburn criticized the questions asked nurses in their final examinations. A typical examination included the following questions: discuss symptoms, signs, complications, treatment, and prevention of rheumatic fever; give causes, management, and treatment of prolonged loss of consciousness; give brief accounts of tetany, hay fever, polyuria, polycythemia, and myxedema; and state the uses, doses, and dangers of streptomycin, meperidine, paraldehyde, and vitamin B_{12}. According to the writers such questions might reasonably be asked doctors in a qualifying examination, but not nurses. They do not ensure that a good nurse shall pass and a bad one fail. Should a nurse have to diagnose, treat, and prevent rheumatic fever, or correct a doctor's dose of certain drugs? These questions do not test nursing ability. If nurses have to know as much as doctors in addition to being nurses, then they should be paid in proportion. The writers suggest that such difficult questions are asked because they are easier to mark. They blame the doctors who prepare the questions and the General Nursing Council for permitting them. Since it is hard enough to recruit girls for a career in nursing, it is the height of folly to frighten prospective candidates away with such examination questions as those quoted.

Quinine Oxidase and Liver Disease.—It is known that an enzyme in the liver oxidizes quinine, being specific for the oxidation of the pyridine nucleus, which is present in quinine and nicotinic acid. Roman and Dulmanis believed that the estimation of this quinine oxidase in serum is an easy and reliable biochemical test for parenchymatous liver damage, since this enzyme is derived only from the liver (*Lancet* 2:90, 1959). They estimated the enzyme level by determining the amount of quinine oxidized by spectrophotometry, the oxidation product having an increased optical density. This is determined after incubating a weak solution of quinine with the serum under test. One unit of quinine oxidase is that amount which causes an increase in optical density by 0.001 under the conditions specified. In normal subjects and in diseases in which the liver is not involved there were less than 5 units of quinine oxidase per milliliter of serum.

In 48 patients with infectious hepatitis the quinine oxidase level varied from 7 to 89 units. In a patient with toxic hepatitis it was 25 units, dropping to 12 units a week after clinical improvement. In general, the milder the clinical symptoms the lower the level of quinine oxidase. Of 20 patients with hepatic cirrhosis raised values were found in three, while those in all the others were below 5 units. The authors believed that this test is of value not only in differentiating between toxic or viral hepatitis and obstructive jaundice but also in the diagnosis of infectious hepatitis in patients with general malaise, and as an indication of active parenchymatous liver damage when other tests are inconclusive.

Hypertension After Gestoses.—In spite of extensive literature there is still some difference of opinion on whether permanent and significant hypertension is a frequent sequel to toxemias of pregnancy in women with a normal blood pressure who become pregnant, and on the amount of damage done by toxemia in a woman who is already hypertensive. Gibson and Platt made a four-year follow-up study of 446 patients who had preeclamptic toxemia and whose blood pressure early in pregnancy was normal (*Brit. M. J.* 2:159, 1959). They took the figure of 140/90 mm. Hg as an arbitrary dividing line between normal blood pressure and hypertension during or before the 20th week of pregnancy. From an analysis of the data there seems little doubt that gestoses cause a permanent increase in blood pressure beyond that which can be explained by the passage of years. This was shown by comparison of the blood pressures with those of healthy controls of the same age and sex. Individual differences existed and a number of women with a history of a gestosis showed no permanent rise of blood pressure. Rarely was the rise in blood pressure of an initially normotensive woman sufficient to seriously affect the expectation of life. Only 17 of the 446 women, or just under 4%, were left with a diastolic pressure of over 105 mm. Hg.

A series of 92 women in whom toxemia of pregnancy was superimposed on hypertension was also followed up. The same criteria employed formerly were used. This group also had a rise in blood pressure four to five years later that was higher than could be accounted for by an increase in age alone. There were, however, extreme variations from person to person, and there was little correlation between the height of the starting blood pressure and the ultimate increase in pressure.

Electrocardiograms in Symptomless Men.—Much reliance is placed on the electrocardiogram (ECG) in the diagnosis of cardiac ischemia, particularly when the pain is atypical. In fact, chest pain with an abnormal ECG is often regarded as cardiac in origin. To assess the reliability of the ECG in diagnosis it is necessary to know how often an ischemic tracing is a chance finding in subjects without cardiac disease. Weitzman and Smith investigated the incidence of coronary ischemia in men without chest pain in the group aged 50 to 80 years. This is the group in which the incidence of coronary artery disease is greatest (*Brit. M. J.* 2:162, 1959). Rigorous criteria to exclude other causes of electrocardiographic abnormality were adopted. The subjects studied were 100 male hospitalized patients who had no history of chest or shoulder pain or any type of heart disease and no cardiac enlargement, diabetes, renal disease, syphilis, peripheral or cerebral vascular disease, or arrhythmia. All had a serum cholesterol level under 300 mg. per 100 ml. and a diastolic blood pressure below 90 mm. Hg. A 12-lead ECG (I, II, III, AVR, AVL, AVF, and V_{1-6}) was recorded at rest, and leads V_5 and V_6 were repeated at 2-minute intervals for 10 minutes after exercise unless the subject was not fit for it.

The usual criteria for electrocardiographic evidence of myocardial ischemia were used, namely large Q waves, flattening or inversion of T waves, and depression of the S-T segment at rest or after exercise. Although such S-T and T wave changes are not specific and can be produced by other cardiac conditions and electrolyte disturbances, patients with these changes were excluded. Flattening of T waves alone or S-T depression of less than 1 mm. was not accepted as evidence of cardiac ischemia unless square depression of the S-T segment of greater amplitude followed exercise. Twelve of the 100 ECGs were suggestive of myocardial ischemia, although there was no other evidence of heart disease. Autopsy was performed on 19 patients and 6 of these had had electrocardiographic evidence of ischemia during life. None of them, however, had evidence of coronary disease when the arteries were injected post mortem with bismuth oxychloride and examined radiologically. These findings emphasize the need for care in relying solely on electrocardiography for the diagnosis of chest pain, which may not be necessarily of cardiac origin even if the tracing is abnormal.

In 59 of these men, including 9 with abnormal ECGs, the serum lipoproteins were examined by paper electrophoresis for the presence of an abnormal pre-beta-lipid band, which is stated by many workers to be associated with myocardial infarction. A moderate pre-beta-lipid band was found in 50% and a large pre-beta-band was found in 10% of the patients with no pain and normal ECGs and in healthy men. A large pre-beta-lipid band was observed in 33% of the patients with electrocardiographic evidence of myocardial ischemia, with or without symptoms, but it was also seen in patients with a number of unrelated conditions. Weitzman and Smith believed that where there was marked metabolic disturbance the lipoprotein patterns might also be disturbed, and this must be borne in mind. The lipoproteins are not specific indicators of coronary disease.

Health Service Report.—The Ministry of Health has issued its report on the National Health Service (NHS) for 1958 (Report of the Ministry of Health for the Year Ending December 31, 1958, part 1, 1959, London, Her Majesty's Stationery Office). The total cost of the NHS in England and Wales for the fiscal year ending March 31, 1958, was 1.76 billion dollars, 75% of which was paid by the exchequer. This is an increase of 115 million dollars over the previous year. The balance was paid for out of local taxation, health service charges to patients, superannuation contributions, and payments from compulsory NHS contributions, which were increased just over a year earlier. Slightly more of the cost of the service is now borne by the direct contributions of people of working age. The cost of hospital and specialist services increased in 1958 by 64.5 million to 950 million dollars. This was partly due to the rise in the prices of goods and services, which increased by 3.5%. Wage increases accounted for 28 million dollars. There was increased use of the hospital service. There were 3,889,000 inpatient treatments, an increase of 95,000 over the previous year, without an increase in the actual number of beds. Waiting lists were 443,000, which was about the same as in 1957. Hospital beds were allocated to the various specialties in the following percentages: mental conditions, 44.3; surgical, 14.8; medical, 14.7; chronic sick and geriatric, 12; obstetric, 3.7; general practitioner units, 2.1; gynecologic, 2; convalescent, 1.6; and miscellaneous 4.8. Private patients occupied 1.2% of all hospital beds. In 1958 the average weekly cost of caring for an inpatient with an acute condition in a London teaching hospital was $93 and in the provinces $75. The average cost throughout the country in nonteaching hospitals was $33.33.

The number of general practitioners working as principals increased from 19,343 to 19,599, and 13,253 were in partnership, or 291 more than in 1957. The average number of patients per doctor was 2,267, which was about the same as in 1957. The number of prescriptions dispensed by pharmacists fell by 4 million, but their cost, which was 184 million dollars was 11.6 million dollars more than in 1957. This was attributed to an increase in the average prescription cost of 75 cents to 90 cents and to the introduction of newer and more expensive drugs. The more expensive antibiotics and steroids made up 34% of all drugs dispensed by pharmacists. The reduced number of prescriptions for the year was explained by the absence of any major epidemics and by the imposition of a prescription charge on all patients. More women had their confinements at home in 1958. The number of domiciliary confinements attended by midwives was 265,215. This was 9,468 more than in 1957. Doctors were present at only 44,964 of these, although they were engaged to attend 220,823.

Less than half (44.5%) of the babies under one year of age received primary vaccination against smallpox. At the end of 1958, 46.7% of the children under 15 years of age had been immunized against diphtheria and 470,290 against whooping cough. By the end of the year about 6 million children aged 15 or under had received two injections of poliomyelitis vaccine. This represents 60% of all children in this age group. The response to free vaccination against poliomyelitis by those in the age group 16 to 25 and by expectant mothers was disappointing. In his comments on the use of the health service the Minister of Health stated that the public is too preoccupied with disease, drugs, and hospitals. The country and the individual would gain if people thought more of preserving good health and acted on the advice given them on how this can be achieved.

Menière's Syndrome.—A new operation performed by Dr. R. B. Lumsden of the Edinburgh Royal Infirmary for the relief of Menière's syndrome was televised at the joint BMA-CMA Meeting at Edinburgh. The object was to destroy the function of the semicircular canals by ultrasonic vibrations without impairing hearing. The canals were exposed by chipping away the mastoid bone. Electric vibrations of about one million cycles per second were converted into ultrasonic vibrations by a special crystal of quartz and directed as a fine beam on the semicircular canals for about 30 minutes. This destroyed the epithelium lining the canals, inactivated the labyrinth, and relieved the vertigo, but did not impair hearing, although over-exposure can permanently damage the seventh cranial nerve.

Lumsden offers operation only to those patients who have failed to benefit from medical treatment and are physically and socially handicapped by their disease. The operation is performed under local anesthesia and the patient is made drowsy with an intravenous injection of meperidine. It is essential that the patient remain conscious as the seventh cranial nerve is tested by asking him from time to time to contract the facial muscles. So far 22 patients have been operated on by this method with complete relief in 13 and improvement in 4. A deterioration of hearing to the extent of 10 to 20 db. occurred in five patients. Histological studies on cats showed that exposure to ultrasonic vibrations caused degeneration of the neuroepithelium of the semicircular canals, but in the dosage used to cause this the organ of Corti was left intact.

Cancer Education.—The first traveling unit in Britain for giving information on cancer recognition and treatment is being launched by the Manchester Committee on Cancer. It will visit factories, offices, stores, and workshops. A specially trained nurse will travel with the van, which is equipped with cine-projector, collapsible screen, films, and literature. The nurse will give talks and show films to groups of workers and answer their questions. Such a program should have economic advantages for industrial and commercial firms. Every trained worker who seeks advice too late for curable forms of cancer represents a needless loss of skill and man-hours.

The committee is an independent voluntary body. Its educational project, started in 1951, now serves 2,500,000 people. The annual report on the project says that a public opinion poll showed a notable improvement in the number of women who believed that cancer could be cured, 55% at present as against 36% in 1953. The number of those who thought early treatment increased the chance of cure had risen from 57% to 71%. There was no comparable improvement in towns not included in the educational project.

Pharmacists Warned of the Danger of Escapist Drugs.—The Council of the Pharmaceutical Society of Great Britain issued a statement to pharmacists warning them of the dangers of the indiscriminate use of escapist drugs acting on the central nervous system. Many of these are obtainable in the drug store without a doctor's prescription and are not subject to legal control. The council warned that drugs that stimulate or depress the central nervous system might lead to habit formation or even to addiction in some patients. Tolerance is rapidly developing to many such drugs, so that they are taken in increasing doses which might lead to changes in character and behavior detrimental to both the patient and society. Some time lag between the introduction of new drugs and the control of their sale by legislation is probably inevitable, but the council believes that, in general, drugs stimulating or depressing the central nervous system should not be supplied on request to the public.

A knowledge of the use of drugs dealing with conditions of stress or taken for their euphoric effects is widespread among the public, owing to modern advertising, and pharmacists are often under pressure to supply such drugs to patients who are not taking them under medical supervision. The council stated that this could only bring discredit to pharmacists, if by the indiscriminate sale of such drugs they encouraged the belief that the stresses of life could be escaped or evaded by the use of drugs instead of being faced and surmounted. A list of 29 drugs that were not, but should be, subject to legal control was issued by the council.

Inoculation Recording by Tattooing.—Norman Lake of Charing Cross Hospital (*British Medical Journal*, Aug. 8. 1959) stated that with an increase in immunization programs the need for some method of indelibly recording the protection in a readily available manner is receiving much attention. In the case of tetanus inoculations, it is important that the record be permanent and on the person of the patient because (1) many years may have elapsed since the inoculation, which in any case, if performed in infancy, is beyond the patient's memory, (2) the patient may be unconscious, and (3) it is routine practice in many hospital receiving rooms to give antitetanic serum for all types of injury, even minor ones, in which the skin is penetrated. The only way of satisfying these requirements is by tattooing.

The desirable characteristics of such a tattoo are that it must be obvious when looked for and yet not conspicuous, and this immediately raises the question of position, for the site should be standardized, hidden, and yet easily available for inspection. The lateral aspect of the great toe, the inside of the lip, under cover of the ear over the mastoid, over the hip just below the iliac crest have all been suggested as possible sites, but the latter position seems, on the whole, the most suitable. Clearly, if the method is adopted the site and size of the mark would have to be established at a national or better an international level.

The author devised a tattooing instrument about the size of a fountain pen. It is in effect a spring gun which on being released drives a "bullet" through a paste of dye for a predetermined distance into the skin. The best dye for this purpose is ordinary commercial lamp black mixed to a paste with a little water and sterilized by heat. The bullet itself, the needle points of which alone penetrate the skin, can be sterilized by boiling or chemically by immersion in chloroxylenol in alcohol. A little of the paste is applied to the cleaned skin of the area, the bullet is inserted into the muzzle of the gun where it is held by a light spring, and the plunger is withdrawn to its full extent. The gun is applied firmly to the skin and the trigger is pressed. The tattooing is instantaneous and practically painless. The depth of penetration (usually 2 or 3 mm.) is controlled by adjustment of the screwed cap and depends on the thickness of the skin at the selected site and on the age of the patient.

Extra bullets (with other designs if necessary) can be accommodated in the hollow head of the plunger. Needle points prepared from stainless piano wire by grinding gave a better tattoo than the highly polished and smooth commercial article. The tattoo consists of a series of dots arranged in the form of a T, is easily identifiable but not conspicuous, and, like all tattoos, is permanent. It is probable that a tattoo performed in infancy will stretch with the growth of the child, but, although sufficient time has not elapsed to observe if this is so, it seems unlikely that it will be enough to render the mark unrecognizable.

Biochemical Diagnosis of Pheochromocytoma.—Vanilmandelic acid (VMA) has been identified as a major metabolite of both epinephrine and levarterenol and comparatively large amounts are excreted in the urine of patients with pheochromocytoma. Sandler and Ruthven developed a precise colorimetric technique for the assay of VMA (*Lancet* 2:114, 1959). This depends on its conversion to vanillin which is assayed colorimetrically. The urine is passed through a cation-exchange resin and the absorbed VMA eluted with acetate buffer, extracted with ethyl acetate, and after evaporation of the latter converted into vanillin by heating with sulfuric acid in the presence of activated alumina as a catalyst. The vanillin is then assayed colorimetrically with indole in the presence of orthophosphoric acid. Patients with pheochromocytoma were found to have a urinary output of VMA from two to six times that of the normal subject. Except for bananas, which contain appreciable quantities of levarterenol, no dietary restrictions need be imposed in performing this test.

Radioactive Corpses.—A panel set up at the request of the Ministry of Health to advise on the disposal of radioactive corpses reported that the hazards associated with tracer amounts of radioactive materials used for diagnostic purposes are negligible in cadavers. Apart from temporary implants, therapy with radioisotopes is virtually confined to the use of P^{32}, Au^{198}, and I^{131}. The panel suggests that hospital physicists should be responsible for advising on radiation problems associated with the disposal of radioactive corpses and with postmortem procedures. When patients who have received therapeutic doses of radioisotopes are discharged from the hospital their doctors should be informed, and cremation, embalming, and autopsy should not be performed without reference to the hospital where treatment was given. No special precautions are necessary for morticians involved in the direct burial of such corpses, nor are they for the autopsy or embalming of corpses containing not more than 5 mc. of Au^{198}, 10 mc. of P^{32}, or 15 mc. of I^{131}. Corpses containing more than these amounts should not normally be embalmed.

These maximum figures do not apply to autopsies because of the greater frequency of these, and the continual exposure of the same staff to radiation from the corpses. If an autopsy is done the pathologist should consult with the hospital physicist, who will advise on the degree of radiation likely to be encountered. The panel advised that proper equipment, including rubber gloves, aspiration apparatus, and rubber tubing should be used. No special precautions are necessary for the cremation of corpses containing up to 30 mc. of I^{131} or Au^{198}, or 10 mc. of P^{32}. Temporary implants of isotopes should be dealt with in the same manner as radium containers and should be removed from corpses before removal from the hospital.

Bacillary Dysentery.—P. J. Taylor (*British Medical Journal*, July 4, 1959) treated a series of patients who had dysentery during an epidemic in Cyprus. Alternate patients were given either phthalylsulfathiazole or Streptotriad (a proprietary preparation containing in each tablet 65 mg. of streptomycin, 100 mg. of sulfathiazole, 100 mg. of sulfadiazine, and 65 mg. of sulfamerazine) for six days. The identity of the two kinds of tablet was concealed. In addition, kaolin and morphine mixture (B. P.) was given as required. The patients were seen daily and the duration of diarrhea and relapse rate were noted. After the six days of treatment one rest day passed before the six consecutive daily stools were examined. The author found abdominal colic to be of little value for diagnostic purposes, since only some 55% of the patients had a temperature and this returned to normal in almost every case by the end of the second day. The author found that the cheap compound consisting of three absorbable sulfonamides and a small amount of streptomycin was superior to the single absorbable sulfonamide alone. The same issue contains a report by Falisevac and co-workers of Yugoslavia who corroborated Taylor's findings and also found the mixture superior to much larger doses of streptomycin alone.

How Much Medicine Should the Public Know?—Conflicting answers to this question were given at the British and Canadian Medical Associations' joint meeting at Edinburgh. Prof. D. M. Dunlop (Edinburgh) thought that the public should be educated in the broad principles of health rather than in medical knowledge. He agreed that the medical profession is not in agreement on how much the patient should be told about his disease. This largely depends on the level of his education. What the physician may tell an Oxford don is not the same as he would tell an untutored man. Dr. C. M. Fletcher (London) said that he was in favor of some education of the public and of patients, especially through the medium of television, because what was seen was more likely to be remembered than what was heard. He suggested that doctors could educate the public by describing the normal functioning of the body, paying special attention to the variations of function under the normal stress and strain of life, which might be mistaken by the anxious person as evidence of disease. Dr. Fletcher said that television programs dealing with disease had been criticized by doctors as pandering to the morbid interests of people, and were likely to interfere with the advice given by individual physicians, but he disagreed with this and thought that demonstrations of the achievements of modern medicine would dispel fear and increase confidence in the nervous and apprehensive patient.

Dr. R. Asher (London) said that it was impossible for intelligent persons to take no interest in their bodies. They are bound to form ideas about them and to seek information about health and disease. If medical information is not provided they may, like children, acquire wrong ideas. Some of these may be harmless and others may be harmful. On the other hand, too much information can be given, as in modern medical encyclopedias for the public, which do more harm than good. Dr. Asher thought it wrong for the public to learn from any source about new treatments, because some persons always thought that any new treatment was bound to be effective. He blamed in particular *Reader's Digest*, from which many persons obtained their information of what is new in medicine. Every doctor knows the patient who comes armed with this magazine demanding to have a particular form of treatment. It is better to give information that is cheering or helpful rather than that which does little good, but is frightening or depressing. If the public is aware of modern developments in medicine physicians themselves will see to it that they keep up with recent medical discoveries.

Raynaud's Disease.—At the same meeting, Dr. J. H. Peacock (Bristol) offered a new concept of Raynaud's disease. He has estimated epinephrine and levarterenol levels in the venous blood from the hand in patients with Raynaud's disease before and after sympathetic stimulation. The catechol amines are separated by chromatography and assayed biologically on the rat's blood pressure. They arise from peripheral sympathetic nerve endings and indicate sympathetic overactivity. In patients with thromboangiitis obliterans smoking cigarettes caused a sharp rise in the catechol amines in the blood in the inferior vena cava just above the level of the adrenal outflow.

In primary Raynaud's disease there is a low level of heat production and a low excretion of urinary estrogens and 17-ketosteroids, and a low plasma-bound iodine level. These changes indicate a new concept in treatment. Peacock gives reserpine to block the excessive production of catechol amines and to decrease their concentration in the arterial walls. Liothyronine and anabolic androgens, such as methandriol, are given to raise the metabolic rate and increase heat production. Vasodilator drugs were found to be of little help and difficult to control, and the late results of sympathectomy were unsatisfactory because of the return of vasomotor tone. Patients treated along these lines have been followed for three years, and the effectiveness of treatment proved by the effect on blood flow in their hands.

Electrogastrograms.—At the same meeting, Dr. H. S. Morton described how the electrogastrogram, originally designed for the detection of action currents in the stomach, could be used to diagnose lesions in the small intestine. The patient swallows a small silver chloride electrode, which is connected by thin wires to a modified Sanborn recorder. Its position is identified radiographically. Action currents caused by changes in potential reflect changes in the motility and amplitude of the contractions of the intestine. One of the uses of the electrogastrogram is to see whether vagotomy will be of benefit, because the activity of the intestine can by this means be measured objectively. The effect of new drugs on the motility of the stomach and intestine can be observed from a study of the electrogastrogram. Obstructive tumors and hemorrhage also effect the record. Morton was careful to point out that changes in the electrogastrogram are not pathognomonic of any particular disease and that it is meant to supplement clinical and radiologic examinations, not to replace them.

Hydatid Disease in South Wales.—At the same meeting, Dr. L. R. West (Glamorgan) stated that although hydatid disease is considered rare in Britain there were 149 cases of human infection in South Wales in 1957-1958. The case fatality rate was 9%. The liver was involved in 44% and the lungs in 43%. Dogs are probably the principal source of infection. A random survey of 50 town and country dogs in South Wales showed that 4 were infected. Bovine and ovine infection, which may be another source, has not decreased over the last 25 years. Thus, 0.9% of 23,632 carcasses examined at a Cardiff abattoir in a three-month period harbored hydatid cysts. This was twice the figure found in an examination of carcasses 25 years ago.

Monday Morning Illness.—At the same meeting, the results of an investigation into the epidemiology of Monday morning illness, another name for byssinosis, the occupational disease that affects those exposed to cotton dust, were described by Dr. R. Schilling (London). The disease is characterized by a tight feeling across the chest with dyspnea on starting to work in the cotton factory on Monday mornings, and relief of symptoms when ceasing work. Those in the carding rooms, who are exposed to cotton dust more than other workers in the industry, are affected the most. The incidence of disease varies directly with the amount of cotton dust in the air and with the amount of protein in the dust. The maximum breathing capacity, calculated by multiplying the volume of air breathed out in 0.75 seconds by 40 subjects, was found to fall sharply during the working day in those suffering from byssinosis. This reduction did not occur when they were working away from cotton dust, nor did it happen in workers in other dusty occupations, such as coal mining.

The effect on respiration is not an allergic response because normal subjects, without previous exposure, were affected if they remained in the carding room exposed to the dust for three hours. Workers with a history of prolonged exposure suffered from lung damage. No correlation was found between the bacterial and fungal counts of the air of the rooms that caused respiratory symptoms. Inhalation of dust containing bacteria and fungi by volunteers had no immediate effect on respiration, but cotton leaf dust when inhaled produced the symptoms typical of byssinosis. The substance responsible is water soluble, heat resistant, and probably polypeptide in nature, but has not been isolated. An extract of cotton leaf dust was found to produce contraction of the guinea pig tracheal muscles.

Psychoses in Infancy and Childhood.—At the same meeting, Dr. W. A. Hawke (Toronto) reported that a detailed history, a careful examination of the child, and an appraisal of the parents through interviews and psychological studies were made in 150 cases of childhood psychoses. The parents were generally highly intellectual, with an average IQ of 120 in one group. Many of them had intellectual, artistic, and musical interests. The psychological analysis of the parents in one group revealed that less than 10% were normal, the remainder being moderately neurotic or overtly schizophrenic. In another group of parents 20% were classified as normal, 60% as severely neurotic or schizoid, and 20% as ambulatory schizophrenics, some of whom had been hospitalized. In both groups of parents examined a number of positive family histories of schizophrenia were obtained. It is concluded that children with psychoses are born into families in which there is a significant tendency toward schizophrenic disturbances.

In a number of these families the parents were not successful in life in spite of high intelligence and education. They tended to occupy positions below their potential capacity and their incomes were less than would be anticipated from their training. Many of the parents could not plan or organize a suitable routine for their children. In a number of cases there was a significant disturbance in the early relationship with emotional deprivation of the child. It was concluded that two factors, constitutional and environmental, are present in most cases of psychoses in childhood and tend to reinforce one another. In general, the greater the constitutional factor the poorer the prognosis, since the basic defect is resistant to therapy. The greater the environmental factor the better the prognosis because this factor may be improved by therapy. In some cases where the parents are frankly schizoid or schizophrenic little can be done unless the child is separated from the family.

Spinal Acrylic Inlays.—Immobilization of acutely painful or unstable spinal joints by bone grafts is a logical method of relieving pain, but bone grafting involves lengthy operations and prolonged hospitalization. Rib inlay grafts give satisfactory support for a time but some soften. Knight reported on the use of paraspinal acrylic inlays instead of bone (*Lancet* 2:147, 1959). The use of acrylic for skull reconstruction, inserted when it is of doughy consistency, and hardening in the tissues within 24 hours, has already proved successful, and excites no significant tissue reaction. The degree of hardness resulting compares favorably with that of pressure-heated material.

The powdered acrylic polymer, Kallodent 222, is sterilized by autoclaving in bottles or a metal container. The liquid acrylic monomer is sterilized by filtration. Twenty minutes before the inlay is required one part of monomer is poured evenly over 3.5 parts of polymer. After about 20 minutes the consistency is tested with a sterile spatula. If still tacky it is allowed to harden. Inlays of 1.7 cm. are used in the lumbar spine and half this thickness is used in the cervical spine. An inlay of appropriate size for the cavity exposed is cut from the material and when dry and rubbery it is inserted into the wound. After the insertion of the plastic between the lamina and paravertebral muscles the spine is supported in the optimum position for 24 hours, which allows the inlay to mold itself over the bones. The secret is in having the inlay of the right consistency. If it is too wet a serous effusion may occur.

Knight has used these paravertebral inlays for the relief of spondylosis, osteoarthritis, chronically painful fracture-dislocations, and the stabilization of atlantoaxial subluxations. The effect is produced by reduction in movement at the level of the painful joint. After operation an extremely good range of spinal movement is provided by the joints above and below the site of immobilization. The patient is operated on in a sitting position. Through a midline incision the paravertebral muscles are dissected to expose the backs of the laminae on one side only. After complete hemostasis the inlay is used to completely fill the space over the laminae before the paravertebral muscles are resutured.

Psychosis and Addiction to Phenmetrazine.—Phenmetrazine is a sympathomimetic drug, with an action similar to that of amphetamine, used for the treatment of obesity. Evans treated a series of 16 patients who had become ill from taking the drug in large doses, 12 of whom were addicted to it (*Lancet* 2:152, 1959). Nine had symptoms that were indistinguishable from those of an amphetamine psychosis. They had delusions of a paranoid, nihilistic, and depressive type, hallucinations, and disturbances of affect. Two patients were disoriented. All recovered after hospitalization for a week, but four patients had relapses after discharge and started taking increasing quantities of the drug. The history of an excessive intake of phenmetrazine, a frank psychosis, and its resolution on stopping the drug justifies the term phenmetrazine psychosis.

A second group of five patients had a delayed recovery. All had taken 10 to 20 tablets of phenmetrazine for weeks or months. The symptoms of two of the patients resembled those described. Two had a definite schizophrenic thought disorder with vagueness and bizarre associations. If consumption of the drug is concealed the psychosis due to it cannot be distinguished from other psychoses. Most of the patients were women who had taken phenmetrazine to help them reduce. Others had taken it to restore energy. Thirteen had taken drugs, alcohol, or amphetamine derivatives previously. Their work record was unstable, as all had changed jobs frequently. Three patients said that in certain coffee bars and clubs in London phenmetrazine is used frequently as an energizer. Phenmetrazine is definitely a drug of addiction and it should be obtainable only on a doctor's prescription, which cannot be refilled.

Olympic Games.—Doctors and scientists will accompany the British athletes to the Olympic games in Rome next year. They will help to reduce the effects of exposure to unaccustomed sunlight, heat, and humidity, and help the athletes to adapt themselves to different foods. A drop of only 2% in efficiency can reduce an athlete from the first to the sixth place in the competition. Athletes are prone to gastric and digestive upsets which the doctors attending the team hope to prevent. Suggestions to be considered are that the British team should train for a period in heavy track suits to acclimatize themselves to exercise under hot climatic conditions, and to receive sun-ray treatment before leaving Britain. The Medical Research Council and the British Association of Sport and Medicine will advise on adaptation to new climatic conditions.

Labor Party's Plan for Health Service.—Political parties are always active when a general election is imminent. As another government is likely to be formed this fall the Labor party has produced a new health program which they propose to implement if returned to power. Although there is public concern over the annual cost of the National Health Service (nearly 2,000 million dollars) the Labor party suggests spending another 300 million dollars on it. The details were given at a press conference recently and in a party publication. It is proposed to spend 150 million dollars a year on new hospitals. Capital spending on the hospitals is now running at about 75 million dollars annually, which is about one-third of what the British Medical Association recommended. Labor's argument is that in an expanding economy the proportion of the national income spent on health should rise.

One proposal in the Labor program is that the 21,000 government-paid general practitioners should have fewer patients on their lists than at present. This would be achieved without reducing their income. Labor admits that general practice is the Cinderella of the service and that the general practitioner works hard under intolerable conditions, with his wife as an unpaid worker in the service. About 25% of the population are on the lists of doctors with more than 3,000 patients. Labor's goal is 2,500, although it does not propose how this should be done without more doctors. An appointment system for visits to the doctor's office is proposed because the public wastes millions of hours every year waiting to see general practitioners. Group practice by general practitioners will be encouraged by loans to acquire new offices. Many doctors' offices are still dirty, dingy, and poorly equipped according to the report. All charges for medicaments are to be removed and employers are to pay more toward the cost of their employees' health.

Teaching hospitals enjoy comparative independence at the moment, with their own boards of governors. This will be lost if the Labor proposals are implemented. These hospitals will be integrated with the regional hospital boards. The new order wishes to encourage research, particularly in the nonteaching hospitals, and to extend the industrial health service, which at present is paid for by private industry. Medical education, particularly in London's 12 medical schools, is to be the subject of government inquiry. The Labor party believes that medical education in London is dominated by the views of specialists on Harley Street, and is thus isolated and insulated from the realities of medical work as most doctors have to practice it. The party aims to give further responsibility to regional boards and management committees, and to reduce paper work, meetings, and bureaucracy in the administration of the hospitals.

The present mental health services come under criticism. They have been deprived of money for years the party states. A major building program of psychiatric units in general hospitals is proposed, with extension of the social services for the community care of the mentally sick. Increased facilities for their home care is suggested. A free mobile chiropody service for older persons and a mobile physiotherapy service are also recommended. To remedy the shortage of dentists Labor plans to encourage the recruitment of dental students. In 10 years the nation's drug bill has risen from 98 million dollars a year to 176 million dollars. Labor hopes to reduce this by supplying doctors with information on the nature and price of drugs prescribable under the health service. Doctors would be informed monthly of the cost of their prescriptions to the state, and vigorous attempts would be taken to reduce the price of drugs. It is pointed out that more money is spent on the drugs prescribed than on the doctors who prescribe them. The party considers that private beds in state-owned hospitals are an anomaly, and hopes that they will soon disappear.

More bureaucratic control is promised to doctors in partnership. Permanent assistantships and assistantships without a view to partnership will be made unlawful. All partnership agreements will have to conform to standards laid down nationally and be approved by local executive councils before signing. The Medical Research Council is criticized. Of 840 million dollars a year spent on research in the country, only 22.5 million dollars is spent on medical research. The Labor party considers that the Medical Research Council must revise its approach and create many more research posts so that practical problems may be tackled by large teams. Many of these proposals and criticisms come from a party that forced a hastily conceived National Health Service on an unwilling medical profession, and is itself responsible for some of the shortcomings of the service. The Labor party's criticism of the Medical Research Council is irresponsible. This body does excellent work on its meager budget.

Strontium-90.—The Radiological Laboratory of the Agricultural Research Council has published a report entitled "Strontium-90 in Human Diet in the United Kingdom" (Her Majesty's Stationery Office, 1959). It concludes that the average amount of radioactive strontium (Sr^{90}) in the food and water of persons living in Britain is about 17% of that which would call for action. Some diets include a higher intake than others, but no foods have a content at present considered dangerous. The level recommended by the Medical Research Council above which action should be taken is 40 μc per gram of ingested calcium. At present the average British diet contains 6 μc per gram of calcium.

The danger of Sr^{90} is that it is metabolized in the same way as calcium and deposited in the bones. Although few persons consume diets containing more than 10 μc of Sr^{90} per gram of calcium, diets in certain limited areas may contain as much as 23 μc of Sr^{90}. In these areas the environment would lead to the rapid transfer of Sr^{90} to the diet. Some foods such as whole wheat bread and milk contain a high proportion. Whole wheat flour not only contains more Sr^{90} than white flour, but it has no added calcium carbonate as has the latter. Calcium added to the diet decreases the amount of strontium absorbed as it is taken up preferentially by the skeleton. Sr^{90} is in the fall-out of atomic explosions, although only that which has fallen out in the preceding one or two months is likely to be found in food in any quantity. There is a delay of this period from the time of fall-out to the appearance of Sr^{90} in milk. It is very persistent, the half-life being 30 years.

The delay between the fall-out and the entry of Sr^{90} into the food shows that the amount in the diet is not the result of the accumulation of successive quantities in the atomic fall-outs since 1945, when the first nuclear weapon fell. When it is washed well into the soil it becomes less and less accessible to plants and animals. An increase of Sr^{90} in food and water during the current year is likely because many bombs were recently exploded and it is likely to persist for a time. The report points out that the amount of Sr^{90} absorbed from the food could be decreased by increasing the calcium intake, which could be done by adding it to flour.

CORRESPONDENCE

MICROSCOPIC HEMATURIA

To the Editor:—In the Aug. 15, 1959, issue of The Journal, page 2014, in the Correspondence section, is a statement by Dr. Bruce H. Stewart concerning the number of erythrocytes found in urine and the interpretation of this number. He objects to a widely circulated brochure stating that in centrifuged urinary sediments the normal number of erythrocytes per high-power field varies from 4 to 10. Dr. Stewart concludes "that more than one red blood cell per rare high-power field in a routine centrifuged urinary sediment must be considered abnormal."

It is never possible to give quantitative results from a procedure which is not carried out in a manner designed to yield such results. In neither one of these references is any standard procedure set up for determining the number of cells per high-power field. Actually, even the high-power field is not defined. Some persons examine urine with a 5X ocular, while others use a 10X ocular, and some consider an 8-mm. objective as being of high power while others consider a 4-mm. or even a 3-mm. ocular to be of high power.

The report by Greene at the Mayo Clinic cited in the letter by Dr. Stewart was based on a standard procedure which has been used in the Section of Clinical Pathology for many years. Although the laboratory work itself is rigidly supervised, there is no supervision of the actual collection of the specimens, and these results may be based on anything from a single-passed specimen to a 24-hour collection of urine. This in itself may make a great difference in the number of cells found in a high-power field.

When the urine is delivered to the laboratory, it is shaken and 14 ml. is poured into a 15-ml. conical centrifuge tube. The tubes are centrifuged in a no. 2 International centrifuge with a 16-place, 15-ml. head, at 1,800 rpm, for eight minutes, the time being measured from the moment when the centrifuge has reached its maximal speed. The supernatant is poured off, leaving about 0.5 ml., which is shaken, and then one drop is poured from the centrifuge tube onto a glass slide and a 22-by-22-mm. cover slip is applied. This gives a fairly "thick" preparation. Six high-power fields are counted with use of a 4-ml. objective and a 10X ocular. The numbers of cells in the six fields are averaged to give the count.

It can be seen that any one of a number of factors, if varied, can produce a marked difference in the results. For example, if the preparation is one-half the thickness described above, the number of erythrocytes per field will be reduced about 50%. Variations in the centrifugal force applied to the specimen also will give great variability in the results. It is possible, if the standard used at the University of Michigan Medical School is based on a smaller amount of urine which is centrifuged for a shorter period and with less centrifugal force, and if the high-power field is one obtained with a 5X ocular, for one red blood cell per high-power field to constitute a relatively large amount of blood as compared with the figure which forms the basis for the report by Greene or the figure given in the brochure referred to. Attempts to read laboratory results too finely and too dogmatically have led to many errors, and one should be cautious in taking over the laboratory reports from one laboratory and applying them to another. One swallow still does not make a summer, and one erythrocyte does not make a diagnostician out of a sophomore.

T. B. Magath, M.D.
Section of Clinical Pathology
Mayo Clinic
Rochester, Minn.

DIHYDROSTREPTOMYCIN DEAFNESS

To the Editor:—In The Journal, Aug. 1, page 1657, is an important article entitled "Dihydrostreptomycin Deafness," in which the authors have set down a report concerning 32 cases of deafness occurring after administration of dihydrostreptomycin. This fairly transcontinental study from the four points of the compass in the United States shows the extent to which antibiotics are administered. Penicillin, the first of these, was found to be of tremendous value, but since it did not prove effective in every instance, combinations of antibiotics were used with better results. Then streptomycin, discovered by Waksman, was heralded and it seemed that many sufferers were relieved of tuberculosis, although some patients had impaired hearing or visual disturbances after use of the drug.

Then Glorig, in 1951, reported on the effect of dihydrostreptomycin hydrochloride and sulfate on the auditory mechanism (*Ann. Otol. Rhin. & Laryng.* 60:327-335 [June] 1951), an initial contribution which had to do with tuberculous patients who had received this drug in doses of 2 to 7 Gm. weekly. Irreversible deafness was noted three weeks to five months later. Then came combinations of other antibiotics with such names as Combiotic, Dicrysticin, Distrycillin, Strocillin, and Durycin.

The previously mentioned 32 cases of deafness from dihydrostreptomycin occurred after administration of the drug to patients with cystitis, influenza, tuberculosis, pleural effusion, asthma, nephritis, panhysterectomy, furuncles, respiratory infections, pneumonia, appendectomy, mononucleosis, sinusitis, and encephalitis. The latent effects, especially deafness, came on weeks or months after administration of dihydrostreptomycin in combination with penicillin or other antibiotics. A small dose of dihydrostreptomycin may be sufficient to produce deafness. Both ears are affected equally, and the loss runs from 20 to 70 decibels.

Fifty years ago I began work in otology in the old Politzer clinic in Vienna. The Wassermann test had just come out, and it was claimed that arsphenamine would "cure syphilis at one shot." Many patients so treated became deaf. Clinicians did not know then that it was the impurities in the arsenic which were responsible for deafness. History now seems to have repeated itself.

Irving Wilson Voorhees, M.D.
35-26 79th St.
Jackson Heights 72, N. Y.

COMPLICATIONS FROM CHLORPROMAZINE

To the Editor:—The account by Floch and Leibowitz in The Journal, Aug. 22, 1959, page 2060, entitled "Hemorrhage from Multiple Sites Associated with Chlorpromazine-Induced Jaundice" adds yet another to the long list of complications resulting from the use of chlorpromazine. The comment concerning the appearance of hyperglycemia in the patient under discussion indicates that this was believed to be an independent finding related to a coincidental occurrence of diabetes mellitus. It may be worthwhile to point out that the hyperglycemia in question may not be an independent and accidental occurrence of diabetes mellitus but may, in fact, be due to the chlorpromazine.

Hiles, in The Journal, Dec. 29, 1956, page 1651, described a number of patients who developed hyperglycemia and glycosuria while receiving chlorpromazine. In some of these the effects disappeared after the cessation of the drug therapy. Charatin and Bartlett published a report, abstracted in The Journal, Sept. 10, 1955, page 145, on an investigation into the hyperglycemic effect of chlorpromazine in man. It would be of interest to know whether the patient described by Floch and Leibowitz is still considered diabetic or whether the hyperglycemia was transient.

George X. Trimble, M.D.
Director of Medical Education
Seaside Memorial Hospital
Long Beach, Calif.

The above comment was referred to the authors of the article cited, and the following reply has been submitted.

To the Editor:—The comment by Dr. Trimble is of interest. The observation of fasting hyperglycemia early in the course of our patient with chlorpromazine-induced jaundice led to the performance of a glucose tolerance test on the 10th day of her illness. This was typical of diabetes mellitus. It was duplicated when the test was repeated on the 42nd day after the onset of illness when all evidences of liver dysfunction had disappeared and she had long abstained from the drug. Available follow-up information failed to clarify whether this hyperglycemia and abnormal glucose tolerance were transient or persistent. No similar data have been obtained thus far since her discharge. At no time did random urine samples reveal glycosuria, either during the illness or in the follow-up period. There was no diabetic history prior to the illness and no family history of diabetes. In preparing our paper we were at first struck by the apparently frequent occurrence of diabetes mellitus in reported cases of chlorpromazine-induced hepatitis as well as in patients we had previously observed, but when these were actually counted we could find no greater incidence than chance would explain. It is for that reason that we concluded that the diabetes mellitus was an independent coincidental finding.

Sidney Leibowitz, M.D.
15 W. 54th St.
New York 24.

HYPERURICEMIA

To the Editor:—I have read with interest the paper on the relationship of hyperuricemia to hypercholesteremia and acute myocardial infarction by Kohn and Prozan (*J. A. M. A.* 170:1909-1912 [Aug. 15] 1959). The authors implied that the hyperuricemia seen in their patients was a hereditary defect and gave no information as to other possible causes of hyperuricemia in this group. Hyperuricemia may be due to several causes other than heredity. The most common is chronic renal insufficiency. It would be of great interest to learn the frequency of blood urea nitrogen elevation among the 50 patients reported on in this paper. Also information should be given as to the possible presence of blood dyscrasias that are associated with hyperuricemia (Talbott: *Medicine* 38:173 [May] 1959; Gutman: *Ann. Int. Med.* 39:1062 [Nov.] 1953). Finally, in a group of patients with acute myocardial infarction, it is possible that some were receiving chlorothiazide for either congestive heart failure or hypertension. Laragh and others (*J. A. M. A.* 166:145-152 [Jan. 11] 1958) have shown that this drug causes uric acid retention. Even if none of these factors is operative in the patients reported on by Kohn and Prozan, such negative information is important and should have been included in the paper.

Stanley L. Wallace, M.D.
1122 Ocean Ave.
Brooklyn, N. Y.

THE LEISURE CORNER

COLLECTING OF MUSICAL BOWS

When a Frenchman named Françoise Tourte perfected the art of bowmaking in the late 1700's, he introduced into the musical world a device that has become the magic wand of many musicians. Everyone knows that the violin, the best known and mostly widely used of all string instruments, requires a bow, which is usually a curved stick about 27 in. long, containing about 150 horsehair threads stretched from the tip to an adjustable frog. The musical tones of the violin are made by pulling the bow back and forth over the strings. It was Tourte who lengthened the bow, reversed its curve, and made it lighter and more willowy than the earlier types of bows had been. The first bows were curved like the weapon of the same name. The bow probably originated in the Orient, and was introduced to Europe during the Crusades.

The earliest use of bows on stringed instruments is shrouded in mystery. Whether a stringed instrument was first played by plucking or bowing is still undetermined, although it is generally maintained that plucking had precedence. Ancient Persians always plucked their instruments, while some of the Asiatic peoples such as the mountain and island dwellers of India "bowed" their instruments. It was not until the Persians eventually came into contact with other races that they became acquainted with the use of the bow. In like manner, the inhabitants of the shores of the Mediterranean Sea learned to pluck their instruments, while the Gothic peoples, chiefly Germanic in origin, identified their urge for musical expression with the use of the bow. The earliest bow, which dates back to about 1000 A. D., resembles a branch; it appears as a pliable reed held in a bent position by threads, strings or horsehair, tied at each end.

It was not until the 17th century, when the violin evolved into its present form, that more accurate and definite information about the bow was introduced. Henry Saint-George, author of "The Bow," has this interesting comment to make: "I wonder whether violinists often realize when they take up a bow how many remote parts of the earth have contributed to this little magic wand! Wood from the West, ivory from the East, mother of pearl from the sea, gold or silver from eastern, western, or it may be Antipodean mines; and when we add thereto the hair from the horse's tail, and we levy a tax upon the three kingdoms, vegetable, animal and mineral, to minister to our enjoyment." As for construction of the bow, the greatest concentration of precious wood employed in making fine bows is found in the forests of Pernambuco, one of the coastal regions of Brazil. In addition to the utilization of Pernambuco wood and brazilwood, the woods probably most commonly used in bow-making are derived from beech and snakewood. The markings one sometimes sees on bows, wherein the grain resembles the splotches or rings of a snake, identify the source of material. Ebony is still another type of wood employed in the construction of a bow, but this is second in importance to Pernambuco wood, which is often selected because of its hardness and its ability to resist wear.

Many doctors have become collectors of bows used in conjunction with the violin, viola, violoncello, and double bass. The hobby frequently consists in selecting bows that were built many generations ago right down to those constructed at the present time. As in the case of the hobby of collecting valuable paintings, a bow made by a good maker, in excellent condition, with perfect mountings, and possessing a fine playing quality becomes a valuable possession. Prices commanded by bows depend on construction, craftsmanship, and design. Collectors are known to look for fine bows all over the world. They seek a graceful tapering of the stick, the proper length, elasticity and flexibility, the precise balance of size and weight of head and frog, the proper method of fastening the hair with ferrule and slide at the frog so as to hold it in a flat ribbon, the exact fitting of frog to stick. Each one of these details in a bow is conceived and executed with meticulous care, exactness, and artistry.

Doctors do not necessarily have to be accomplished musicians themselves in order to appreciate the considerable artistry that goes into the making of a superb bow. When purchasing a bow as a collector-hobbyist or a musician or both, it is well to investigate the condition of the bow, with attention paid to certain details; for example, the presence or absence of cracks in the head, tip, shaft, and frog. Indeed, the stick should be straight and devoid of bad knots or other imperfections, while the frog should sit closely and accurately to the stick. Since an increasing number of people have evinced growing interest in bows in recent years, the value of a bow as a work of artistic construction and as an important musical-playing adjunct has become more widely recognized. More expert concern, as a result, has developed among dealers, musicians, connoisseurs, and collectors.

The cost of a fine bow, made by an "old master," has like all other items in our economy, mounted. At the beginning of the 20th century seven excellent bows by Françoise Tourte commanded a catalogue price ranging from $125 to $300. Today, a good Tourte bow is rarely offered for sale, and even when it is obtainable the price is at a premium. Similar high prices hold true for bows made by such fine makers as Vuillaume, Dodd, Lupot, Eury, and Voirin. Fine examples of their work are scarce, yet at the same time they are more appreciated, since appreciation of fine construction has grown. The increased scarcity of exceedingly fine bows is due to the fact that some of them have been broken over the years, while others have been damaged beyond repair.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Postviral Myopericarditis Associated with the Influenza Virus: Report of 8 Cases. C. W. Adams. Am. J. Cardiol. 4:56-67 (July) 1959 [New York].

During the influenza epidemic of 1957-1958 the author observed 8 patients with acute "nonspecific" pericarditis, who had a fourfold rise of serum antibodies against the influenzal virus. The latent period of one or more weeks between the acute influenzal attack and the pericarditis suggests that an allergic or a hypersensitivity mechanism is involved. The laboratory evidence demonstrated in 5 cases the type B (Great Lakes) influenza virus; in 2 cases both type A (Japanese) and type B viruses; and in 1 case the type A virus. Acute "nonspecific" pericarditis is not necessarily "benign," as it is frequently associated with myocarditis, pericardial effusion, pleurisy, pleural effusion, and pneumonia. These features may be more appropriately designated as acute myopericarditis.

Seven of the 8 patients presented were males. One patient was a woman in whom the pericarditis occurred at the time of delivery and during the postpartum period. For many years, instances of "postpartal heart disease" have been reported without a previous history or clinical findings of heart disease. In fatal cases, the myocardium has shown moderate infiltration of lymphocytes and macrophages. It has been pointed out that "postpartal heart disease" is probably not due to a specific entity or even necessarily related to pregnancy or the puerperium, but may be related to one of a number of different etiological agents. All patients with "postpartal heart disease," atypical myocardial infarction, or acute "nonspecific" pericarditis should be carefully evaluated for the recent presence of viral diseases as a possible cause of the cardiac difficulty. The hemagglutination inhibition influenzal antibody titer determinations are recommended in all cases of acute "nonspecific" pericarditis in an effort to further classify these cases. The history and the clinical and laboratory findings in these 8 cases of "nonspecific" pericarditis suggest that this cardiac disorder is, in fact, a myopericarditis, and the term "postviral myopericarditis" is suggested in preference to acute benign "nonspecific" or "idiopathic" pericarditis.

Effects of Lanatoside C on Cardiovascular Hemo-Dynamics: Acute Digitalizing Doses in Subjects with Normal Hearts and with Heart Disease Without Failure. D. T. Dresdale, Y. Z. Yuceoglu, R. J. Michtom and others. Am. J. Cardiol. 4:88-99 (July) 1959 [New York].

Patients with heart disease but not in failure are frequently considered for prophylactic digitalization prior to major surgery or other types of unusual stress. If no deleterious effects on the cardiovascular hemodynamics are demonstrated, such therapy might well be justified. This report presents the early effects of lanatoside C on the cardiovascular hemodynamics in 11 patients studied by the technique of right heart catheterization. Seven of the 11 patients had normal hearts, and the other 4 patients had heart disease without clinical or hemodynamic evidence of heart failure. Lanatoside C in full therapeutic doses caused no significant changes in cardiac output, heart rate, systemic venous, right ventricular systolic, and pulmonary artery pressures. The systemic arterial pressures and resistances similarly were not appreciably affected. In 2 of 8 cases, there was a slight fall in the right ventricular end-diastolic pressure, and in 5 of 6 cases there was a slight fall in right auricular pressure. Interpretations of the presented data were made on the basis of control studies, but it is pointed out that there are difficulties in interpreting the changes in cardiac output in this type of study.

The problem of whether prophylactic digitalization is useful in patients with heart disease but not in heart failure was not solved by this study. Nevertheless, it is felt that these patients can be digitalized without fear of decreasing cardiac output or producing unfavorable changes in blood pressure.

Heart Disease and Influenza. G. Bourne and J. Wedgwood. Lancet 1:1226-1228 (June 13) 1959 [London].

The authors present observations on 14 patients, observed during the 1957 epidemic of influenza, in whom influenza appears to have been the cause of cardiac disability. Auricular fibrillation was pre-

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The place of publication of the periodical appears in brackets preceding each abstract.

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cipitated in 8 patients, and auricular flutter in 1. Symptoms of coronary artery disease were initiated in 2 patients. Two other patients with angina of effort due to coronary artery disease, who were being studied by serial exercise tests, became worse after an attack of influenza. Their angina became more severe, and objective evidence of deterioration was obtainable from exercise tests. Finally, in one patient influenza seems to have caused an inversion of the T wave in the left ventricular leads, but this reverted to normal during convalescence.

After describing the case histories of the 14 patients, the authors point out that in 4 of the 8 patients with auricular fibrillation there was no evidence of any other cardiac abnormality; in the other 4 the electrocardiogram revealed signs of an underlying myocardial defect. In the patient with auricular flutter the abnormal rhythm seemed to be due entirely to the acute influenzal infection. Influenza appeared to initiate angina of effort in 2 of the 4 patients with coronary symptoms, and to accentuate the ischemic state in 2. In these latter 2 patients influenza also increased the electrocardiographic abnormality. In the last case the long history of premature beats, and later of paroxysmal tachycardia, pointed to some chronic but slight cardiac abnormality. Thus, in 6 of the 14 patients influenza would seem to have caused definite cardiac complications, and in the other 8 to have brought them to the surface. The ages of the patients, ranging from 47 to 70 years, with an average of 57, suggest that in all of them the heart may not have been perfectly normal. Influenza appears to have a definite, although transitory, toxic effect upon the myocardium.

The Incidence of Arteriosclerotic Heart Disease Among Cirrhotics. J. B. Berrios and R. C. Rodriguez. Bol. Asoc. méd. Puerto Rico 51:205-211 (June) 1959 (In English) [Santurce].

The material for this study was selected from 3 sources: records of 1,276 autopsies performed at the Bayamón District Hospital in Santurce, Puerto Rico, during the period 1955-1958, and records of 2 groups of patients treated at the same hospital. Five groups of subjects were studied. Group 1 comprised 66 cases in which the cause of death had been arteriosclerotic heart disease. The average age of the patients at death was 66.5 years. There was no record of Laennec's disease among these cases. Group 2 comprised 9 cases in which the cause of death had been Laennec's cirrhosis. The average age of the patients at death was 41.5 years. There was no record of arteriosclerotic heart disease among these cases. Group 3 comprised 100 records of autopsies taken at random. There were 20 cases in which arteriosclerotic heart disease had been the cause of death, and among them only one patient had also had hepatic cirrhosis. Group 4 was composed of 84 patients with the clinical diagnosis of cirrhosis of the liver. The mean age in this group was 52.5 years. Nine patients (10.7%) in this group had also arteriosclerotic heart disease. Group 5 was composed of 50 patients taken at random from among those who had been given a diagnosis of arteriosclerotic heart disease at the Bayamón District Hospital. The average age in this group was 67.8 years. None of these patients had concomitant hepatic disease.

Comparing the respective incidences of the two diseases in the groups under study, it was found that the incidence of arteriosclerotic heart disease in the groups with a diagnosis of hepatic cirrhosis (10.7%) was much lower than the percentage of incidence in the general Puerto Rican population (25%). This finding also tends to show that cirrhosis of the liver may protect the patient against atherosclerosis. This "protection" is attributed to the changes in lipid metabolism which take place because of diffuse parenchymal hepatic disease, with consequent lowering of plasma cholesterol and phospholipids. If the findings in this study are corroborated, they may also explain the low incidence of atherosclerosis among the Oriental and Bantu populations who have a high incidence of liver disease.

Cytological Diagnosis of Sputum with Feulgen's Test in Cancer of the Lung: Note II. G. Angrisani, G. Curzio and S. Musella. Acta med. ital. 13:151-158 (June) 1958 (In Italian) [Rome].

Early morning sputum derived from spontaneous cough of 50 patients with pulmonary disease was subjected to Feulgen's test. Thirty-four patients had or were suspected of having pulmonary carcinoma, 12 had pulmonary abscess, and 4 had bronchiectasis. Feulgen's test was positive in 31 of the 34 patients with pulmonary carcinoma. The authors believe that in the other 3 patients the anatomic location of the tumor was responsible for the negative results. A round-shaped neoplastic mass at the base of the superior right lobe was seen on roentgenographic examination in 2 of these patients, but cytological examination, which was repeated 5 times, always gave negative results. Anatomic examination of the lung after surgical removal showed an intraparenchymatous tumor formation, small in size, with no lesion of the large and medium bronchi. Only a small bronchial branch, closely connected with the peripheral area of the neoplastic tissue, presented light ulceration of the mucosa and infiltration of the other layers. No other significant histological involvement of any bronchial lumen was present in these 2 patients. The third patient had a bronchial adenocarcinoma. Histologically the adenocarcinomatous proliferation did not invade the bronchial surface; the bronchial mucosa covered the tumor that protruded into the bronchial lumen. In this patient, too, the authors believe that the negative results of the cytological test may have been due to the absence of neoplastic exfoliative cells in the bronchial lumen.

Carcinoma was discovered through Feulgen's test in 4 of the other patients who on roentgenologic examination had presented a pulmonary suppuration. The authors point out that a good feature of Feulgen's test is that it eliminates the most serious errors due to false positivity. Negative results of the test in patients with carcinoma of the lung may be connected with the process of exfoliation of the tumor, or they may be the result of a transient occlusion of the air passages, clogged with mucus, which is likely to occur in cases of regional inflammation.

Pneumonia in the Aged. J. C. Gerrits. Nederl. tijdschr. geneesk. 103:1109-1112 (May 23) 1959 (In Dutch) [Amsterdam].

The clinical course of pneumonia has become milder. Particularly in elderly persons it frequently takes a milder, atypical course, but it nevertheless may terminate in death. Staphylococcic pneumonia, so often observed in the course of influenza epidemics, takes a definitely atypical course. Among 69 pneumonia patients in whom the author made bacteriological studies, 39 had pneumococcic pneumonia, 15 had a mixed bacteriological flora, 4 had pneumonia due to Staphylococcus aureus, and the remaining 11 patients had mostly Hemophilus influenzae and Streptococcus organisms.

The author is concerned with studies on the duration of pneumonia, which he investigated in 313 patients who were observed from July, 1955, to July, 1957, at 2 Amsterdam hospitals (170 receiving hospital treatment, and 143 being observed at the polyclinic). Since observations on younger patients had demonstrated that resolution of the pneumonic process is usually complete within one month, the author classified the patients not only with regard to age but also according to the time elapsed between onset and recovery. Fifty-two of the patients died, all but 5 of the deaths involving persons over 50 years of age. Disorders of circulation and respiration were frequent in the patients who died, but the nature of the causative organism apparently was of no importance. In 154 of the 261 surviving patients, the course was prolonged beyond one month. Retardation of recovery was especially frequent in patients over 50. In this age group recovery required more than a month in 75% and more than 2 months in 32% of the patients, whereas in patients under 20 the comparative percentages were 32 and 12%. Delayed recovery was chiefly due to respiratory disorders (bronchitis, asthma, or emphysema) or to circulatory disorders (myocardial degeneration, arteriosclerosis, and mitral stenosis).

The Treatment of Allergy to Ragweed Pollen by Means of a Single Annual Injection of Emulsified Pollen Extract: VI. Discussion of Results, Relationships and Some Miscellaneous Factors. E. A. Brown, Ann. Allergy 17:358-379 (May-June) 1959 [St. Paul].

During the year 1958 Brown treated 1,029 patients who had disorders caused by allergy to ragweed pollen. Of these, 344 received either from him, or under his supervision, standard pollen extract prepared in isotonic sodium chloride solution and given according to the multiple visit type of injection program. (Observations on the 344 patients will be presented in a separate report.) The other 685 patients were treated with a single preseason injection of an emulsified pollen extract, the emulsifying agent consisting of 1 ml. of Falba and 1.5 ml. of mineral oil (liquid petrolatum) for 0.5 ml. of pollen extract. Falba is an emulsion stabilizer which (according to Loveless) contains beeswax, paraffin oils of varying viscosities, and oxycholesterins extracted from lanolin. Atreol no. 9 U.S.P. is a light mineral oil. The 685 patients were subjected to a special study in order to establish the efficacy of the emulsified extract. Some of these patients had seasonal pollen asthma and others had both hay fever and asthma. In approximately half of the population (335), the disorder had been present for up to 10 years, and in 218 more for 11 to 20 years.

Symptoms of some type were observed during the ragweed pollen season in 113 of the treated patients, but in only 56 of these could exposure to pollen alone be incriminated. In another 57, an allergen other than pollen, acting alone or cumulatively with ragweed pollen or other allergens or pollens, resulted in symptoms which occurred during the period of ragweed pollination. The symptoms observed occurred in patients who, by intracutaneous and conjunctival tests, had responded with wheals, pseudopodia, and flares to 4 different test levels. They were treated with doses which were based on the arbitrary assumption that the tests indicated the amount of pollen extract to be injected. There was evidence that in the 35 patients treated before May 1, and in the 23 others who took their injections after August 1, symptoms were noted with greater frequency. But no matter when the injection was given, the patients who received smaller doses apparently did not do as well as the others. This may be a result of the small dose injected, or else due to the fact that it takes less exposure to pollen for such patients to respond with symptoms. For the following year, some such patients will receive the same dose (booster principle), some higher doses (higher dose–higher protection principle), and some, a less denaturalized pollen extract (incomplete protection principle).

The patients who reported for treatment after August 1 could not have been treated at any other time, but for 1959 they will be given injections on dates earlier in the year. The patients treated before May 1 will be given their injections at a later date. The patients allergic to other pollens will be given protection for both. All patients presenting symptoms (without exception) did better than they had done for the previous year, which was one of lesser pollination. But in 113 patients some symptoms, whether mild or subjective, were noted; 56 of these were treated with dexamethasone, and some of the others with mild antihistaminic agents. In the remaining 572 patients treated by means of a single injection of emulsified extract, there were no symptoms whatsoever. From the results seen, it can tentatively be concluded that the emulsion injection treatment represents a major breakthrough in the treatment of human pollinosis.

The Allergic Nature of Essential Hypertension. A. F. Coca. J. Appl. Nutrition 12:69-70 (no. 2) 1959 [Los Angeles].

Coca challenges the definition of the term "allergy" as "an abnormal state caused by the specific interaction of antigen and antibody in a susceptible tissue or organ." The antigen–antibody mechanism was assumed to exist in all conditions of specific sensitivity even when sensitizing antibodies could not be found. It has been adhered to despite the fact that it was disproved by the observation that most adult patients fail to give satisfactory skin reactions to allergenic foods (allergic antibodies being absent). Gay, who was the first to identify essential hypertension as a manifestation of specific sensitivity, emphasized that skin testing, although valuable in inhalant allergy, is not a reliable diagnostic method in food allergy, as there is a high percentage of false-negative and false-positive reactions. He based food testing on Vaughan's "postdigestive leukocyte response," the so-called leukopenic index. Gay also adopted specific tachycardia, the pulse test, as a criterion of an allergic reaction, and later defined it as the method of choice for the study of all manifestations of food allergy, including essential hypertension.

Treatment of Respiratory Acidosis. O. Storstein, T. Elgvin and R. Rokseth. Tidsskr. norske laegefor. 79:667-673 (June 1) 1959 (In Norwegian) [Oslo].

In chronic diffuse pulmonary diseases, destruction of larger amounts of lung tissue and insufficient ventilation of the alveoli will make the lungs unable to renew the blood gases. Anoxemia and hypercapnia result. Anoxemia is, as a rule, the first sign of pulmonary failure. Later the carbon dioxide content in the arterial blood also increases, and respiratory acidosis occurs. The reduced arterial oxygen saturation causes a central cyanosis. In the chronic cases described, the narcotic effect of carbon dioxide becomes evident. The important basic disease is emphysema due to chronic bronchitis, and the acute deficiency is often precipitated by an acute infection. Two of the 6 patients reported on had acute pneumonia; 4 had cor pulmonale. The results of blood gas analyses were decisive for diagnosis and treatment. All the patients were given oxygen, usually by nose catheter. In case of doubt as to the possible harmful effects of oxygen, it was given by nose catheter in a weak stream for half an hour followed by an hour's pause; if no tendency to hypoventilation was seen, the stream was increased.

It is important for the physician to be aware of the possibility of hypoventilation and carbon dioxide narcosis and to be ready to administer some form of artificial respiration in patients with alveolar hypoventilation. Increased carbon dioxide accumulation leads to increasing carbon dioxide narcosis, and the patient dies. If the carbon dioxide excess can be removed by increased lung ventilation and the patient can be brought to a normal carbon dioxide pressure in the arterial blood, his respiratory center will react normally to carbon dioxide stimulus, and he will be free from symptoms for months and years. The disastrous effect of oxygen and morphine is shown in the first case reported; the patient fell into a coma after the combined administration and died within a few hours without being given artificial respiration. Two patients died of cor pulmonale.

Acute Promyelocytic Leukemia: Study on 20 Observations. J. B. Mathé, J. Boulay, B. Céoard and J. Chomé. Schweiz. med. Wchnschr. 89:604-608 (June 6) 1959 (In French) [Basel, Switzerland].

The authors report clinical, hematological, and anatomic observations made during the last 20 years in 20 patients with acute promyelocytic leukemia. The ages of the patients ranged from 15 months to 75 years, but the majority of them were less than 20 years old. The onset of the disease in these patients was sudden, and the course was short. The disease was characterized by the infrequent occurrence of lymph node or spleen enlargement and by the frequency of hemorrhagic manifestations related not only to thrombocytopenia but also to accelerated fibrinolysis. All the patients showed, besides extensive hemorrhagic manifestations, severe anemia resulting in tachycardia, dyspnea, or cardiovascular disturbances. Adenopathies were present in 10 of the 20 patients, and manifestations referable to the bones in 7. Inflammation of the nasopharynx with a fibrinoid necrotic reaction was present in one patient, and necrosis of the wing of the nose in another. Fever was present in all the patients at the time of admission to the hospital. The results of the examination of the bone marrow were characterized in all the patients by a hyperplasia of promyelocytes associated with a general increase in cells. The patients were treated with cortisone or other steroids, but, except for one patient who had a transient remission, the course of the disease was rapidly progressive, and the patients died. Promyelocytic leukemia and myeloblastic anemia can easily be differentiated by the cytologist, whereas a differential diagnosis between acute promyelocytic leukemia and a certain bone marrow aplasia in which the bone marrow shows an increase in the number of promyelocytes is more difficult to establish. Anatomic lesions found at autopsy are on the basis of promyelocytic hyperplasia, infiltration of the viscera with these cells, and hemorrhagic phenomena.

Further Observations on the Combined Cortisone-Antibiotics Therapy for Infectious Diseases; in Particular, the Therapy with Intravenously Administered Cortisone. R. Scalabrino. Minerva med. 50:1578-1588 (May 23) 1959 (In Italian) [Turin, Italy].

The author reviews his experience with the combined preparation of hydrocortisone sodium succinate, corticotropin (ACTH), and antibiotics in the treatment of certain infectious diseases. Hydrocortisone and ACTH are administered intravenously. The combined preparation can reduce the mortality rate in the following conditions: certain severe infectious diseases characterized by a high degree of hyperergia and toxicity and accompanied by marked neuroendocrinic stupor; diseases in which there is a considerable degree of involvement of the adrenals, such as the Waterhouse-Friderichsen syndrome, highly acute sepsis in childhood, and the adrenal variety of brucellosis; acute episodes of asthma associated with insufficiency of the right ventricle; cerebral apoplexy: surgical shock and in bilateral adrenalectomy; infections or severe traumatic "stresses" which develop in the course of long-term cortisone therapy; some varieties of blood disease; and the acute phases of rheumatic and collagenous diseases. The combined preparation can also shorten the course and attenuate the toxic effects of sepsis in older persons. An additional advantage in administering hydrocortisone intravenously is to produce immediate effects, whereas those produced by other routes are slower. The author suggests decreasing the dosage of hydrocortisone, although no standard rule can be set regarding the dosage and duration of treatment with the combined preparation.

Epidemic Hemorrhagic Fever Investigation in the T'uliho Area, Inner Mongolia, and Clinical Study of 104 Cases. F. H. Ch'iu, T. C. Hou, P. S. Huang and others. Chinese M. J. 78:515-531 (June) 1959 (In English) [Peking].

During an epidemic outbreak of acute infectious disease in the T'uliho area of Inner Mongolia in 1955, the authors observed 198 patients who had been given a preliminary diagnosis of epidemic hemorrhagic fever. The diagnosis was confirmed in 80 typical and 24 atypical cases that constitute the subjects of this report. Of the typical cases, 68 patients were men and 12 were women; they included all ages, with a predominance of young adults. In 60% of the typical and 75% of the atypical cases the patients were in the 20-to-39-year age bracket. Although the clinical manifestations of this disease vary tremendously, the course of the typical cases was marked by the succession of 5 phases, which are designated, according to signs and symptoms predominating in each, as febrile, hypotensive, oliguric, diuretic, and convalescent. The basic pathological changes in epidemic hemorrhagic fever are extensive damage and dilatation of the capillaries and increased fragility and permeability of the capillary walls, with consequent hemorrhages and plasma transudation, fall of blood pressure, hemoconcentration, and several complicating pathophysiological changes. According to the data collected by the team of specialists who made a coordinated study of the T'uliho outbreak, a virus is possibly the causative agent; wild rodents are the most likely reservoir hosts, and mites the vectors.

No specific treatment has yet been found for epidemic hemorrhagic fever. Antibiotics were administered to the patients in the T'uliho outbreak without any noticeable effect. The general management of the cases reported here consisted of isolation of the patients during the first 10 days of the illness; disinfection of blood and urine specimens; a diet high in carbohydrates and vitamins, low in protein and salt; treatment of the specific symptoms and complications as they occurred in the individual cases. Of the 80 typical cases studied, 71 patients recovered. The main causes of death in the 9 fatal cases were shock, uremia, and acidosis. All the patients with atypical epidemic hemorrhagic fever recovered. Follow-up studies were carried out in 95 cases for 1½ to 2 months after recovery. In 9 patients symptoms of the diuretic phase were still present, and a few patients still suffered from mild headache, dizziness, and weakness. The authors call attention to the need of differentiating epidemic hemorrhagic fever from other acute febrile infections, blood disorders such as hemorrhagic and allergic purpura, and kidney diseases. The differential diagnosis is established by etiological and serologic studies.

Functions of Testes and of Adrenal Cortex in Acute Hepatitis and Cirrhosis of the Liver. H. Voegt and O. Weller. Deutsche med. Wchnschr. 84:1093-1096 (June 12) 1959 (In German) [Stuttgart, Germany].

Men with cirrhosis of the liver often show signs of androgen deficiency. Not only is there a reduction in body hair, but the external genitalia decrease in size, potency and libido decrease, and gynecomastia may develop. The authors investigated the hormonal and spermatogenic functions of 8 men with cirrhosis of the liver and of 10 men with severe acute hepatitis. The results of the tests in these patients were compared with those in healthy men. It was found that in the presence of acute or chronic damage to the parenchyma of the liver the hormonal and spermatogenic functions of the testes decrease. The reduction is more marked in cirrhosis than in hepatitis. The duration of hepatitis determines the degree of abnormal testicular function. The testicular insufficiency is due to the fact that the anterior pituitary produces less gonadotropin, and this, in turn, is caused by an increase in circulating estrogens and a fall in amino acids and vitamins as a direct result of the liver damage. After the acute hepatitis regresses, the secondary hypogonadism subsides, and the testicular functions return to normal.

Urinary aldosterone excretion is increased to 2 or 3 times the normal value in acute hepatitis and compensated cirrhosis. In decompensated cirrhosis of the liver the urinary aldosterone excretion rises further after the ascites fluid is removed by paracentesis. The concentration of the Porter-Silber chromogens in plasma and urine is greatly reduced in patients with hepatic cirrhosis. In severe acute hepatitis there are no definite abnormalities in the 17-hydroxycorticoids. Functional tests of the adrenal cortex by means of injections of corticotropin (ACTH) indicate that the hypocorticoidism is secondary, that is, it results because the liver disease diminishes the formation of corticotropic hormone.

Primary Carcinoma of Liver. M. Joselevich and Z. Markus. Prensa méd. argent. 46:173-177 (Jan. 16) 1959 (In Spanish) [Buenos Aires].

Two patients, 77 and 54 years old, respectively, with primary carcinoma of the liver were observed. The symptoms appeared in one 2 months and in the other 3 weeks before hospitalization. Both patients complained of marked weakness, hypochondriasis on the right, epigastric and hemithoracic pain, rapidly progressive hepatomegaly, loss of weight, gastrointestinal disorders, and ascites which was of fibrinous type in one patient and hemorrhagic in the other. In the first patient, the symptoms were those of cirrhosis of the liver with jaundice and fever. A clinical diagnosis of hypertrophic cirrhosis of the liver was made. The disease followed a rapid course with final hepatic coma. The patient died 17 days after hospitalization. An autopsy showed massive primary carcinoma of the liver (originating in the intralobular bile canaliculi) and metastases to the regional lymph nodes and to the kidney. In the second patient, the symptoms were those of a tumoral liver. Puncture biopsy of the liver showed hepatoma. No autopsy was permitted.

The Kidney in Macroglobulinemia of Waldenström. P. Michon, G. Rauber, A. Larcan and F. Streiff. Presse méd. 67:1267-1270 (June 24) 1959 (In French) [Paris].

The authors studied 7 patients with macroglobulinemia of Waldenström and reviewed 200 cases of this disease cited in the literature. The analysis showed that macroglobulinemia is frequently associated with renal manifestations which are similar in many respects to those observed in patients with multiple myeloma and also in other pathological states, such as cryoglobulinemia and atypical dysproteinemia. Laboratory findings in patients with macroglobulinemia of Waldenström may show mild azotemia, albuminuria, or variable globulinuria, and sometimes Bence-Jones albumosuria indicating subacute nephritis. The similarity in the clinical, biological, anatomic, and physiopathological aspects of these renal anomalies accompanying other major dysglobulinemias suggests that all should be classified in one group, i. e., as dysglobulinemic nephropathies. This new entity should be kept in mind in treating patients exhibiting certain forms of renal insufficiency, and the tests needed to establish the diagnosis should be made.

Kanamycin Treatment of Chronic Bronchitis. F. Hahnemann and I. Gragsted. Ugesk. læger 121:879-881 (May 28) 1959 (In Danish) [Copenhagen].

Twelve patients with acute flare-up of chronic bronchitis were treated with kanamycin; in most cases a disappearance of Pfeiffer's bacilli was demonstrated, but there was no certain clinical improvement. Like other investigators, the authors found no renal or vestibular injury, but there was injury of the auditory nerve in 3 cases. Kanamycin is considered unsuitable for the treatment of chronic bronchitis, especially in patients with reduced renal function.

SURGERY

Treatment of Tumors of the Parotid. R. Funder. Tidsskr. norske laegefor. 79:663-666 (June 1) 1959 (In Norwegian) [Oslo].

Salivary gland tumors in the parotid are of considerable interest because of the high frequency of recurrence closely related to inadequately performed primary operation. Between 150 and 200 such tumors occur in Norway annually. They are mainly salivary gland mixed tumors and are regarded as potentially malignant due to their tendency to recurrence and later transition into malignancy. If the entire capsule, which consists of compressed parotid tissue, and a sufficiently large part of normal parotid tissue are not removed together with the tumor, there is danger of recurrence from the capsule. Total parotidectomy would be ideal. Most frequently subtotal parotidectomy is done in the case of benign mixed tumors, with abundant resection at a good distance from the tumor. In malignancy most authors advise radical parotidectomy without regard to the facial nerve. Selective staining of the parotid gland with a methylene blue solution is advantageous. From 1956 to 1959, 22 operations for parotid tumor were performed at the Rikshospital in Oslo. The average duration of the tumors was 6 years—4½ years for the benign tumors and 15 years for the carcinomas. The average age of the patients was 43 years. Women predominated. The tumors were almost twice as frequent on the left side. Local pain was present in the affected area in 7 of the 19 patients with benign tumors. Primary operation was done on 16 patients with benign tumors, and 3 patients were operated on for recurrence after earlier operation, with subtotal parotidectomy in 18 cases and enucleation of the tumor in 1 case. Two of the 3 patients with carcinoma were operated on radically; one patient refused operative treatment.

Surgical Therapy of Strokes. F. R. Denman. Texas J. Med. 55:563-567 (July) 1959 [Austin].

Denman emphasizes that about 40% of the patients with neurological syndromes simulating stroke have atherosclerotic occlusion of the internal carotid or vertebral arteries in the neck, rather than of the inaccessible intracranial vessels. Cerebral function depends upon a balanced arterial flow through the 4 major cervical trunks and their intracranial branches. Atherosclerotic plaques developing at points of origin of the internal carotid and vertebral arteries narrow the lumen and produce complete occlusion. Thrombo-occlusive disease of the cervical carotid or vertebral arteries is clinically characterized by rapidly or slowly progressive syndromes, featuring blindness and hemianopsia, aphasia, sensory and motor disturbances, convulsion, coma, headaches, memory loss, and confusion or senile dementia. Three clinical syndromes may be recognized: 1. The onset may be explosive and result in the clinical pattern of a fully developed stroke. 2. There may be recurrent episodes of a very transient nature lasting from a few moments to hours and followed by complete or partial recovery for some time before a catastrophic event occurs which produces severe disability or death. 3. A slowly progressive course may be associated with headaches, paresthesias, irritability, memory loss, and mental deterioration.

The occurrence of any of the symptoms should arouse suspicion of caroticovertebral stenosis or occlusion. Inequality of the carotid pulsations is suggestive. Absence of carotid pulsation in the neck indicates occlusion of the common carotid. The presence of a localized systolic murmur over the carotid bifurcation in the absence of a transmitted cardiac murmur indicates a partially occluding lesion. Of special usefulness in diagnosis is the measurement of retinal artery pressures bilaterally. The pressures are low on the side of carotid artery occlusion. Final diagnosis can be made only by angiography or direct exploration. Angiography should be carried out promptly in all patients with symptoms of cerebrovascular insufficiency, to determine the exact anatomic distribution of vascular occlusion, if any, and to assess the status of the collateral circulation.

Since the atheromatous lesions are essentially segmental in nature, they are amenable to arterial reconstructive techniques. In general, 3 methods have been utilized: (1) thrombectomy and thromboendarterectomy; (2) resection and graft or direct union; and (3) bypass procedures by graft or end-to-side union of the external carotid to the internal carotid. All these methods have their application, but because exposure of the distal portion of the internal carotid artery is limited for graft purposes, thromboendarterectomy is frequently most feasible. If surgery is carried out before thrombosis becomes irremovable or brain damage becomes irreversible, excellent results may be obtained, and a significant number of patients will be salvaged.

The Open Correction of Rheumatic Mitral Regurgitation and/or Stenosis with Special Reference to Regurgitation Treated by Posteromedial Annuloplasty Utilizing a Pump-Oxygenator. K. A. Merendino, G. I. Thomas, J. E. Jesseph and others. Ann. Surg. 150:5-22 (July) 1959 [Philadelphia].

The authors of this report are concerned with the valvular involvement of rheumatic fever, which results in mitral regurgitation, alone or in combination with stenosis. They describe certain relationships of the annulus-valve complex in the competent and the incompetent mitral valve and clinical experiences in patients with mitral regurgitation and/or stenosis secondary to rheumatic fever. They also describe posteromedial annuloplasty, an operative procedure found to be of value in the correction of mitral regurgitation. Having performed the first successful operation utilizing annuloplasty in October, 1956, they report observations on 10 patients: 4 with pure mitral insufficiency; 4 with mitral insufficiency and/or stenosis; and 2 with mitral disease and aortic insufficiency. As regards functional capacity and clinical status, all 10 patients belonged to either class 3 (the 4 with pure mitral insufficiency) or to class 4 (the remaining 6). The operation was performed under direct vision with the aid of a pump-oxygenator. As experience has been gained and changes in equipment have been made, permitting larger flows during bypass, the postoperative convalescence has become similar to that of patients undergoing blind commissurotomy. The diminution in, and often the total absence of, all murmurs and the reduction in heart size, together with the subjective and objective evidence of improvement, have been most encouraging.

Experience to date indicates that disabling pure mitral regurgitation is accompanied by a large left atrium, a mobile valve without calcium, and a dilated annulus. When the diameter or circumference of the atrioventricular canal is reduced by posteromedial annuloplasty, regurgitation is corrected. The combined lesion of mitral stenosis and regurgitation is characterized by a mild to moderate enlargement of the left atrium, a badly deformed valve with calcium, a shortening of the posterior cusp, and a mild to moderate dilatation of the annulus. After correction of the stenosis by commissurotomy, a limited posteromedial annuloplasty may correct the associated regurgitation. No substitute for valve substance was attempted in this series. The simple maneuver of forcibly elevating the anterior and posterior cusps, grasped by clamps, proved invaluable in identifying the "chordal gate" for commissurotomy.

The authors call attention to maneuvers which tend to lessen the danger of air embolism. Packing the mitral valve area prior to the removal of atrial thrombi appears to be an aid in preventing the systemic embolization of fragmented clots. Thrombi were encountered only in pure mitral stenosis. The mortality of open mitral valve surgery, while high, is approaching the risk of blind commissurotomy in patients of class 4 clinical status. However, the presence of aortic insufficiency, though of secondary hemodynamic importance to the mitral disease, presently constitutes a more serious prognosis. Both of the patients in whom mitral disease was associated with aortic insufficiency died, whereas one each of the other 2 groups of 4 died. Because of the seriousness of even minor degrees of aortic regurgitation, and the inability preoperatively to distinguish between aortic and pulmonic insufficiency, a tie-tape is now routinely placed about the aortic root for control, if needed, in all cases. As this experience represents a learning phase in open surgery of acquired rheumatic valvular disease, it is expected that, with additional experience, errors will be avoided and the risk in future operations will be less.

In an addendum the authors state that, since submission of this paper, 21 patients have been operated on, and this additional experience supports the validity of posteromedial annuloplasty. Best results have been obtained in patients with pure mitral insufficiency; those with mixed stenosis and insufficiency presented the most difficult technical problems.

Analysis of a Case of Constrictive Pericarditis. O. Fustinione, H. Ruggero and I. J. Corsini. Prensa méd. argent. 46:165-169 (Jan. 16) 1959 (In Spanish) [Buenos Aires].

The authors analyze a case of constrictive pericarditis with a 15-year-long course during which ascites constituted the only sign or symptom. Other atypical features in the case were an enlarged heart and an almost normal heart beat. The patient, a 60-year-old man, had been hospitalized 15 years before because of an enlarged abdomen. He had left the hospital one month later, after having undergone 3 abdominal punctures with withdrawal of 8 to 10 liters of fluid at each puncture. Subsequently 3 other punctures had been performed. The patient had been bedridden for several months before rehospitalization. When first seen by the authors, he had been given a diagnosis of hepatic cirrhosis and was scheduled for surgical intervention. All preliminary examinations had been unrevealing. Subsequently laparoscopic findings, as well as the histological examination, suggested the presence of cirrhosis. A new radiogram of the chest, taken in the oblique anterior position, showed an area of calcification around the left ventricle. A radiologic investigation was then carried out in a search for further signs of calcification. Catheterization of the heart showed marked elevation of pressure in the right chambers and reduction in the volume of the systemic circulation. The existence of extensive calcification was confirmed, and the diagnosis of constrictive pericarditis was established.

The patient was treated on a low-salt diet and with mercurial diuretics, digitalis, vitamins, and liver extract; abdominal paracentesis gave temporary relief to the ascites. After 2 months of this treatment, there was improvement of the edema and dyspnea, but the ascites remained unchanged. A surgical intervention was then carried out, the patient being under anesthesia with Pentothal, ether, and intravenously administered Novocain, and with tracheal intubation. The heart was covered with a thickened pericardium; the calcification zones had invaded both ventricles and the openings of both venae cavae. Pericardiectomy was performed, with complete decortication, under direct vision. The surgical intervention was followed by marked general improvement, disappearance of the ascites and edema, decrease in the engorgement of the cervical veins, and increase in the differential blood pressure and the diuresis. The psychic status was also much improved. The patient was able to walk again, although the exercise caused him some dyspnea and palpitation.

The Triad of Congenital Absence of Aortic Arch (Isthmus Aortae), Patent Ductus Arteriosus and Interventricular Septal Defect—A Trilogy. E. A. Everts-Suárez and C. P. Carson. Ann. Surg. **150**:153-159 (July) 1959 [Philadelphia].

The authors believe that one of the least common, if not rarest, congenital anomalies of the aorta is absence of the arch. They performed an autopsy on a 3-day-old male infant in whom this abnormality was present, accompanied by a defect in the interventricular septum and a patent ductus arteriosus. They also found records of 16 cases of congenital absence of the aortic arch (theirs included), 13 of which were associated with an interventricular septal defect and a patent ductus arteriosus. Regarding the clinical findings, patients with this condition have cyanosis of the lower portion of the body and a normal upper portion. They also show cyanosis on the left, with normal color of the upper right extremity, when the defect occurs distal to the origin of the left common carotid artery but proximal to the origin of the left subclavian artery. These findings, however, have been recorded only occasionally. Some of the symptoms described are dyspnea, cyanosis during feeding or crying, heart murmurs, engorgement of hand veins, weakness and limpness after 24 hours of life, and hepatomegaly.

The possible explanation for the survival of these patients for at least 24 hours, and up to 11 days, appears to be the polycythemia present in infants at birth, the amount of oxygen transported to the tissues being relatively adequate. With the postnatal decrease in the blood count, there is an increase of tissue anoxia which apparently precipitates the death of these infants. The embryologic explanation for the defects is discussed. It is the authors' contention that this entity represents a vascular trilogy not previously discussed as such. It should be brought to the attention of the medical profession and particularly to cardiovascular surgeons.

Atypical Approaches to the Mitral Valve Because of the Impracticability of Approach through the Left Auricular Appendage. C. A. Carlon, A. Jovine and G. Giuliani. Acta chir. ital. **15**:373-389 (May-June) 1959 (In Italian) [Padua, Italy].

The classical approach through the left auricular appendage in performing mitral commissurotomy was not feasible in 21 patients out of more than 600 with mitral stenosis. The approach through the wall of the atrium was made in 15 patients and through the pulmonary veins in 6. Hypoplasia or aplasia of the left auricular appendage, or dilation and thin walls of the atrium, contraindicated the standard approach. A new blade for finger fracture procedure, which was devised by one of the authors, was used with ease and successfully in these operations. The blade has the shape of a nail and is firmly attached to the tip of the finger by a double clamp, being tied securely by 2 long threads with the ends coming out of the glove. The blade has 3 sharp edges, one on the distal side and 2 on the lateral side. This implement makes possible a continuous and uninterrupted procedure in exploring the atrial cavity and mitral orifice and in performing mitral commissurotomy; it thus obviates the necessity of first exploring the mitral orifice with a bare finger, and then reintroducing it with the instrument. The surgeon can precisely resect the commissures by moving the 3 sharp edges of the blade in a saw-cut instead of a rotating fashion. The sharp distal edge cuts through the glove and thus disengages the sharp edges of the blade as soon as the operator presses harder against the mitral orifice. In the series reported, no operative or postoperative death attributable to the technique took place.

A Survey of 102 Patients With Bronchogenic Carcinoma at the Togus Veterans Administration Center. P. F. Lansing, J. Maine M. A. **50**:247-250 and 261 (July) 1959 [Portland].

The author investigated the records of 102 patients with a diagnosis of bronchogenic carcinoma, who were hospitalized between June, 1948, and February, 1957. The average age of the patients was 60 years. The majority of them had noted symptoms, such as cough, weight loss, hemoptysis, chest pain, and chronic pulmonary disease, less than 3 months prior to hospitalization. Of 81 patients in whom the quantity of cigarette smoking was noted, 64 had smoked from 1 to 3 packs a day for 30 to 50 years. Metastases to other organs at the time of initial evaluation were suspected in 10 patients and definitely diagnosed in 27; the condition was present but was missed in 5 patients. Metastases developed during the course of illness in 33 patients; the condition was present but was missed in an additional 3 patients. Jaundice was present during the course of illness in 5 patients.

Forty-one patients whose disease was not considered inoperable were subjected to thoracotomy: on 15 of these pneumonectomy was performed, on 3 lobectomy, and on 14 exploratory thoracotomy alone; tumor removal at thoracotomy, including all lymph nodes, was considered to be complete in 9 patients. Carcinoma was considered inoperable in 45 patients. One patient refused surgery. In 7 patients surgery was inadvisable because of advanced age, severe heart disease, and severe debility. In 8 patients no surgery was undertaken because of poor pulmonary function. Nine patients received one course of nitrogen mustard. X-ray therapy was given to the majority of patients for palliation; one patient received a cancerocidal dose. Three patients were treated with both nitrogen mustard and x-ray therapy; of these one patient had a superior vena cava compression syndrome.

The time of survival from the first day of hospitalization was less than 3 months for 52 patients. Six of the 15 patients who underwent pneumonectomy survived 2 years. Among the group who received x-ray therapy, there were 2 patients who survived 2 years. Only one of the untreated patients survived 2 years. One patient who had a pneumonectomy with incomplete removal of hilar lymph nodes survived 5 years and is presumably still living. At the conclusion of the survey in February, 1957, there were still 4 living survivors; the time of survival in 6 patients was unknown. The poor survival of this group was considered to be due to the high incidence of metastasis which was present at the time of diagnosis and which also developed during the course of the illness. It is emphasized that the histological type of a cancer is the most important prognostic feature. In this series the survival of patients with epidermoid carcinoma was twice as long as the survival of those with anaplastic carcinoma.

Lung Biopsy for Obscure Pulmonary Lesions. C. C. Craighead. J. Louisiana M. Soc. 111:256-261 (July) 1959 [New Orleans].

The author reports on 3 men and 2 women, between the ages of 30 and 57 years, on whom thoractomy with lung biopsy was performed at the Charity Hospital of Louisiana and the Flint Goodridge Hospital in New Orleans. The operation was accomplished under local or general anesthesia through a small anterior chest incision, with little morbidity and a short stay in the hospital. The pathological processes revealed by the procedure were pulmonary fibrosis, pulmonary metastatic malignancy with impairment of alveolar-capillary diffusion (so-called alveolar-capillary block syndrome), pulmonary alveolar proteinosis, psittacosis, and aspergillosis. The wide variety of pathological processes observed in the lung is verifiable only by histopathological and biological differentiation, and biopsy of the lung may be necessary to uncover the cause. Studies on the roentgenograms, while usually typical of the disease, overlap in their identities to the point that other aids must be used. Treatment without a diagnosis is often ineffective and may on occasion be dangerous. If an exhaustive survey has failed to yield the underlying pathological process, thoracotomy should be undertaken. Lung biopsy is a dependable diagnostic aid. Two indications for lung biopsy exist: to verify the diagnosis and to establish medicolegal documentation in occupational disease.

Pulmonary Resection for Mineral Oil Granulomas. L. D. Guidry, O. T. Clagett, J. R. McDonald and O. W. Kincaid. Ann. Surg. **150**:67-75 (July) 1959 [Philadelphia].

Previous reports on exploratory thoracotomy and pulmonary resection for mineral oil granulomas masquerading as bronchogenic carcinoma attest to perplexities in diagnosis and treatment occasioned by their deceptive appearance. The authors present observations on 11 patients (7 men and 4 women) on whom pulmonary resection was performed for mineral oil granulomas at the Mayo Clinic since 1947. The average age of the patients was 56 years, with a range of 47 to 70 years. Eight patients were evaluated for suspicious-appearing lesions detected on routine roentgenograms of the thorax; roentgenograms in the remainder were obtained for evaluation of symptoms referable to the thorax, namely, chronic cough and night sweats in the first instance, pleuritic pain in the second, and wheezing, pleuritic pain, and mild dyspnea on exertion in the third. Of the entire group, 6 patients gave histories of chronic cough productive of sputum, which the patients attributed to either heavy smoking or sinusitis with postnasal drip. Seven patients used mineral oil (liquid petrolatum) regularly for regulation of the bowels; 2 used it in the form of oily nose drops for chronic sinusitis; and 2 used it for both chronic constipation and sinusitis. A preoperative history of use of mineral oil was elicited in only 4 instances.

Bronchoscopy disclosed abnormalities in only 3 of the 10 patients on whom it was performed. In all cases bronchial secretions, sputum, or bronchial washings were cultured for pathogens and examined for malignant cells. Droplets of mineral oil were detected in the bronchial washings of 1 of the 2 patients who were suspected of having mineral oil granulomatosis. The presence of a pathological process in one or both lungs was evident in the roentgenogram of the thorax in each of the 11 cases. The lesions ranged in size from 1.2 to 8 cm. in diameter. In 4 patients the lesions appeared as rounded, well-circumscribed masses, while in 7 patients they conformed more or less to the segment or segments involved and had poorly defined borders that faded peripherally. The latter presented roentgenographic features often indistinguishable from other types of pneumonitis. The "spun-glass" appearance, described as characteristic of mineral oil pneumonitis or granulomatosis, was present in 3 of the cases. In 4 of the 11 cases the roentgenologic diagnosis was probable bronchogenic carcinoma. In 4 others the disease process was considered most likely to be of an inflammatory nature, and in 3 patients the roentgenologist suggested the possibility of aspiration of lipid. In no patient could the possibility of neoplasm be safely excluded on the basis of the roentgenologic findings.

Exploratory thoracotomy is advocated for disease indistinguishable from bronchogenic carcinoma, regardless of whether or not mineral oil droplets can be detected in the sputum. Excision is favored for symptomatic or extensive pulmonary involvement when this can be accomplished without excessive sacrifice of normal lung tissue. The establishment of diagnosis should precede any contemplated resective procedure.

Intrathoracic Neurogenic Tumors in Infants and Children: A Study of Forty Cases. O. Schweisguth, J. Mathey, P. Renault and J. P. Binet. Ann. Surg. 150:29-41 (July) 1959 [*Philadelphia*].

The 40 pediatric patients reviewed were observed either in the Gustave Roussy Institute, which is a referral hospital for malignant disease, or in the clinic of thoracic surgery of the Hospital Laënnec, a general hospital in Paris. There were slightly more girls than boys (23 compared with 17). The ages of the children ranged from 5 months to 14 years. Neurogenic tumors are subdivided into 2 groups: (1) neurofibromas and schwannomas and (2) tumors of sympathetic origin. The first group of tumors occurs only in adults, so that none of the children had tumors of this type. Of the second group of tumors of sympathetic origin, 15 children had neuroblastomas, 7 had ganglioneuroblastomas, and 18 had ganglioneuromas.

Twelve of the 15 patients with neuroblastomas underwent thoracotomy. The tumor dissection was grossly satisfactory in 7 cases; in 4, tumor fragments were left at the upper pole of the lesion; and in 1 case, only an excision of a biopsy specimen was done. Three patients were not operated on: one had generalized disease; one died after laminectomy; and in the third, the thoracic component in an hourglass tumor disappeared after radiation therapy. Of 4 patients with sufficient postoperative follow-up, only one has survived and is well 3 years later. The 18 children with ganglioneuromas all underwent thoracotomy and tumor excision. The results were uniformly successful. Postoperative complications were absent, with the exception of the development of a chylothorax in one child, who recovered completely.

Diverse treatments were employed in the 7 children with ganglioneuroblastomas. One patient was operated on between 2 courses of x-ray therapy and is in good health 15 months after the initial treatment. Another child underwent surgery after 22 days of preoperative irradiation; this patient is doing well 11 months later. Four children had tumor surgery without any x-ray therapy, and of these, one patient had a local recurrence which was not radiosensitive. A second operation necessitated a pneumonectomy. Histological examination revealed anaplastic neuroblastoma. Two patients operated on recently have had postoperative irradiation. The malignant potential of the neuroblastic component in these tumors would seem to be best managed by both surgery and radiation.

The authors advise caution in evaluating the treatment of tumors of sympathetic origin in children. They do not regard their therapeutic procedures as necessarily the best. They advise surgery alone for neuroblastomas in infants under 2 years of age and for all children with ganglioneuromas. Postoperative roentgen-ray therapy is recommended for ganglioneuroblastomas and neuroblastomas in children over 2 years of age.

Surgical Treatment of Thrombotic Occlusion of Aorta and Iliac Arteries: The Leriche Syndrome. J. M. Erskine, F. L. Gerbode, S. W. French III and R. M. Hood. A. M. A. Arch. Surg. 79:85-93 (July) 1959 [Chicago].

The syndrome resulting from the arteriosclerotic obliteration of the lower abdominal aorta is known as the Leriche syndrome, because it was first described by Leriche in 1923. A direct surgical attack on the obliterative process in the form of thromboendarterectomy was first carried out by dos Santos in 1946. Because the surgical treatment is still in the developmental stage, the authors review their observations on 33 patients treated surgically during the period from 1953 through 1957. All the patients had intermittent claudication, but the location of the pain in some persons was more widespread than in others. All had pain in the lower legs, and 94% had pain in the thighs and hips as well; only 48% experienced pain in the lower-back area, and in 6% the pain was unilateral. The distance the patient was able to walk before claudication appeared gradually diminished. Another complaint frequent among male patients was inability to sustain an erection.

The femoral pulses were absent or were very weak in the 33 patients, and the more distal pulses were absent. There was little or no atrophy or color change in the lower legs and feet, and the feet might not even feel particularly cold. Roentgenoscopy usually revealed calcification in the abdominal vessels. Aortograms did not seem to be essential in making the diagnosis or in planning the therapy, but they might be required in special circumstances. The block was complete in most of the patients; it often extended from just below the renal vessels to just above the bifurcation of the common iliac arteries. If the block was limited in extent, a thromboendarterectomy was sometimes carried out; but in the majority of cases a resection with grafting was performed. A bilateral sympathectomy was usually added. The operative mortality in the series reported was 3%, and the results were highly satisfactory, through the follow-up period, in more than 90% of the patients, from both the objective and the subjective point of view.

Late Results After Total Gastrectomy for High Gastric Carcinoma. N. Stensrud. Ann. Surg. 150:63-66 (July) 1959 [Philadelphia].

Total gastrectomy was performed on 160 patients for carcinoma of the stomach at the Rikshospital in Oslo during the period from January, 1947, to February, 1952. The operative technique employed was resection of the stomach, with all surrounding lymph nodes, and of the spleen, followed by esophagojejunostomy. Esophagoduodenostomy was performed in only 2 cases. The pancreas was partially resected in 50% of the cases. Special emphasis was placed on careful dissection of the lymph nodes around the celiac axis. A follow-up of the material was made 2 years ago. Seventeen patients (4 women and 13 men) had lived for 3 years after the operation; the rest were dead. The small group of 17 (10.6%) who had survived for more than 3 years after the first investigation have now been reexamined: 16 of them are still alive; one patient died 6 years after the operation, presumably of cancer. While nearly 90% of the 160 patients died within 3 years after the operation, the prognosis for those surviving more than 3 years is good. Pernicious anemia has developed in all the survivors, but apart from this condition and a moderate dyspepsia, the majority are living an active life, with relatively minor discomforts.

Acute Appendicitis: An Analysis of 1,662 Consecutive Cases. J. R. Babcock and W. M. McKinley. Ann. Surg. 150:131-141 (July) 1959 [Philadelphia].

The authors evaluate observations on all patients with appendicitis who were treated at the Geisinger Memorial Hospital and Foss Clinic, Danville, Pa., from 1936 to 1955. Patients in whom appendical inflammation was present but was not the primary pathological process were excluded. Thus, some patients with perforating neoplasms of the appendix or adjacent intestine, ileocolic intussusception, strangulated hernia, and pelvic infection were not considered. The records of 1,662 patients were analyzed. The group included 3 children, between 13 and 24 months of age, but none less than one year old. Seven patients ranged in age from 80 to 89 years. Analysis of the case records with regard to the duration of symptoms revealed that, of the 397 patients admitted 12 hours or less after onset, only 15 had appendical perforation. When the duration of symptoms was considered in respect to mortality, it was found that no deaths related to infection occurred in patients admitted within 12 hours from the time of onset of symptoms. Patients found to have perforation were admitted from 25 to 48 hours after onset of symptoms, and those who ultimately died of perforation were admitted even later. When the condition of the appendixes found at operation was compared in the 4 successive 5-year periods, it was found that the proportion of appendixes which were either intact or perforated was stable, the percentages of intact appendixes ranging from 77 to 72%.

All the patients were operated on irrespective of possible perforation. Antibacterial agents were first used in 1938. During the first 5-year period 9.5% of the patients received sulfonamide preparations. Penicillin was first used in 1944 (during the second 5-year period), but at first it was given in conjunction with the sulfonamides. Not until the following year did penicillin become the principal antibacterial agent in patients with appendicitis. During the third and fourth 5-year periods streptomycin and the broad-spectrum antibiotics were used more frequently. During the fourth period (1951-1955) 65% of the patients with appendicitis received various antibacterial agents. More than 50% of those who received such treatments had intact appendixes.

Thirty-five of the 1,662 patients died, a gross mortality of 2.1%, but since 4 of these patients were not operated on, the mortality of operated cases was 1.9%. Twenty-six of the 35 deaths were due to peritonitis. Although the refinement and appropriate use of adjuncts, such as intestinal intubation, blood and fluid replacement, and improvements in anesthesia, are noteworthy, the authors feel that the use of antibiotics—penicillin, streptomycin, and the broad-spectrum agents—during the last decade of the study was of major importance, being the principal cause for the marked reduction of morbidity and the near elimination of the mortality of appendicitis.

Sliding Inguinal Hernia in Female Infants. S. L. Gans. A. M. A. Arch. Surg. 79:109-113 (July) 1959 [Chicago].

Among 400 infants and children with 516 inguinal hernias (bilateral in 116), there were 68 girls with 90 hernias. Nineteen of these female patients had sliding inguinal hernias, which indicates that this condition is relatively common. Seventeen of the 19 patients were less than 4 months of age; one was 9 months old; and one returned at the age of 3½ years with a sliding hernia on the left side, after having had an incarcerated sliding hernia repaired on the right at the age of 6 weeks. In the majority of the cases there was no complaint. A mass was palpated in the groin or labium majus by the mother or by the pediatrician during a routine examination. The asymptomatic mass varied in size from 1 to 2.5 cm. in diameter; it was always somewhat movable, and occasionally reducible. In other instances the infant was irritable, occasionally drawing up its legs as if in pain, and the mass was somewhat tender to palpation. In 2 instances there was severe incarceration, with swelling, tenderness, pain, distention, vomiting, fever, and dehydration. The condition must be differentiated from inguinal lymphadenopathy, hydrocele of the canal of Nuck, and male pseudohermaphroditism.

At surgery it has been demonstrated that the fallopian tube and the adjoining part of the broad ligament make up at least a portion of the hernia-sac wall. Usually the ovary is also included, and occasionally a portion of the uterus or the entire supracervical part of the uterus. In most instances the organs involved are normal. The principle involved in surgical treatment is the same as that involved in treating all infant hernias—complete removal and high ligation of the hernia sac. It is the contention of the author that this cannot be done without special handling of the sliding portion of the sac. He makes a 3-cm. transverse incision through the skin and subcutaneous tissues of the lateral portion of the suprapubic crease. The external oblique aponeurosis is incised in the direction of its fibers and retracted, carefully preserving the ilioinguinal nerve. The hernia sac is demonstrated, dissected out, and carefully opened in an area away from the sliding elements. The sac is then incised on each side of the sliding element down to the neck. After hemostasis is secured in the edges, the tongue of the sac, with the sliding element, is tucked through the internal ring into the peritoneal cavity. A silk suture is then placed through the cut edges of the sac, making its circumference complete again. The sac can now be handled in the usual fashion by high ligation and amputation. The author discusses the embryologic background of the anomaly.

Partial Nephrectomy in the Treatment of Renal Tuberculosis. B. di Bello. Acta chir. ital. 15:335-371 (May-June) 1959 (In Italian) [Padua, Italy].

Partial nephrectomy is a useful surgical procedure in selected instances of renal tuberculosis. The author discusses this treatment in 2 patients. One patient, a 17-year-old girl, with a family history of tuberculosis, had a tuberculous process in the right lung 3 months before being hospitalized for renal tuberculosis. The pulmonary process was arrested by medical treatment. Pollakiuria and painful urination were the symptoms of the involved kidney. The intravenous urographic examination revealed the presence of a small tuberculous cavity in the superior end of the right kidney. The diagnosis was confirmed by examination of the material of the subsequent partial nephrectomy (superior end). A combined treatment with isonicotinic acid hydrazide and streptomycin preceded and followed the surgical therapy. A dose of streptomycin was administered topically during the operation. Symptoms of the renal tuberculous process recurred after 6 postoperative months of apparent well-being, which necessitated performance of total unilateral nephrectomy.

The second patient, a 48-year-old man, had pain in the right side of the lumbar region, painful urination, occasional hematuria, and pollakiuria 2 months before hospitalization. The presence of a calculus in an upper calyx of the right kidney was established on roentgenologic examination. The patient underwent partial nephrectomy of the superior pole of the right kidney. The microscopic findings of the resected material demonstrated renal tuberculosis. Streptomycin was given to this patient until discharged. He was well on follow-up inspection a year after the operation.

Myocardial Nutrition After Ivalon Sponge Operation: The Return of a 400 Million Year Old System. A. Vineberg, T. Deliyannis and G. Pablo. Canad. M. A. J. 80:948-958 (June 15) 1959 [Toronto].

The use of Ivalon sponge to relieve myocardial ischemia caused by narrowing or occlusion of the coronary artery has raised some strange questions. Is it possible to turn the mammalian heart back into a primitive heart capable of surviving without coronary arteries? Such a primitive heart is to be found in the hagfish, which has no coronary arteries but receives its nutrition directly from the ventricular lumen, i. e., via channels which originate in the lumina of the heart to enter the heart wall through channels between bundles of muscle fibers. A spongework of vascular spaces nourishes the primitive myocardial fibers by direct contact. Does the mammalian myocardial fiber inherit a 400-million-year-old memory so that, given a proper stimulus, it likewise can take its nutrition directly from the ventricular cavity by loosening its own compact structure to one which is more trabecular and by opening up long-unused channels connecting the ventricular cavity to the interior of the heart wall?

These and other questions are being investigated by the authors in the department of experimental surgery, McGill University, and the department of cardiac surgery, Royal Victoria Hospital, Montreal, Canada. Several years ago, the senior author suggested that perhaps one could supply a framework between the myocardium and pericardium through which hundreds of small vessels could grow. Perhaps something with small canaliculi might be of help. After studies had been made with coral formations and marine sponges, it was suggested that Ivalon sponge, an inert substance, would offer an ideal framework to guide the growth of blood vessels from pericardium to myocardium. In order to obtain the proper conditions for such a growth of vessels, at least 3 factors had to be fulfilled: (1) myocardial ischemia had to be created; (2) the serous lining of the fibrous pericardium and the epicardial covering of the left ventricle had to be removed; and (3) the Ivalon sponge sheet had to be sufficiently thin to permit blood vessels to bridge the gap between the denuded pericardium and the heart muscle. To produce myocardial ischemia, ameroid constrictors were placed around the origins of the anterior descending and circumflex branches of the left coronary artery. (Ameroid is a water-absorbing, casein-like material.) A total of 54 animals were operated on. Of these, 25 were control animals and 29 were treated. After excluding animals with complications, 20 control animals and 22 treated with Ivalon sponge were studied. All but two of the control animals died within 18.8 days, all apparently from myocardial ischemia. Of the animals treated with Ivalon sponge, 19 survived for 3 months or longer.

It was found that, when the epicardium of the left ventricle is removed and a thin layer of Ivalon sponge placed directly on the bared myocardial muscle, blood vessels from the fibrous pericardium grow through the sponge into the heart muscle. Further, there is evidence to suggest that, in addition to affording a scaffolding for blood vessel growth from outside into the heart muscle, the Ivalon sponge tends to open up long-forgotten arterioluminal and perhaps myocardiosinusoidal luminal vessels. In this way a heart treated with Ivalon sponge may theoretically receive its nutrition both from outside and from inside the ventricular chamber. The size and frequency of these openings from the ventricular lumen into the heart wall makes one wonder whether these hearts have actually changed into a 400-million-year-old prehistoric type of heart which lives without coronary arteries and receives its nutrition from the heart chambers.

In an addendum to this paper the authors state that the Ivalon sponge operation alone, or together with mammary artery implantation, has been used in 14 patients. Details of the clinical results are being compiled.

The Relation Between the Nasal-Staphylococcal-Carrier State and the Incidence of Postoperative Complications. H. J. Weinstein. New England J. Med. 260:1303-1308 (June 25) 1959 [Boston].

The author observed 125 patients, most of whom received chest surgery. The patients had been hospitalized for an average period of 4 months before the operation, except those in whom other conditions, such as cancer, were suspected and in whom surgery was done at once. The patients were not given antibiotics unless a clear-cut sepsis was present. All patients with nose cultures positive for hemolytic, coagulase-positive Staphylococcus aureus were subjected to topical application to the anterior nares of a bacitracin-neomycin ointment 3 times a day. The treatment was usually begun about 4 days before the operation and continued through the immediate postsurgical period, being discontinued on the 4th or 5th postoperative day.

Thirty-four per cent of the 125 patients undergoing elective surgery had hemolytic, coagulase-positive Staphylococcus aureus recovered from cultures of their noses. Forty-three per cent of those with positive nose cultures had complications of surgery, as compared to 26% of those with negative cultures. Among those with positive cultures 83% of the complications were infected, whereas 40% were infected in the group with negative cultures. The over-all surgical failure rate was 23.3% in those with positive and 7.3% in those with negative nose cultures. It is pointed out that it has always been good practice to postpone elective surgery on patients manifesting infectious processes. This good practice should be extended to include patients who are potentially infected, in addition to those who are clinically infected.

The Surgical Treatment of Endocardial Cushion Defects. D. C. McGoon, J. W. DuShane and J. W. Kirklin. Surgery 46:185-196 (July) 1959 [St. Louis].

The embryonic division of the heart into its 4 chambers involves the growth and final convergence of the atrial septum, the ventricular septum, and the endocardial cushions. A variety of congenital cardiac anomalies, involving the atrioventricular valves and the adjacent portions of the interatrial and interventricular septums, is believed to result from the defective development of the endocardial cushions. The terminology applied to these anomalies has evolved through an increasing understanding of their anatomy and embryology, a process which left behind a confusing nomenclature. Only after recognition of the fact that the "persistent ostium primum atrial septal defect" is characteristically accompanied by deformity of the atrioventricular valves was it realized that the name was not adequately descriptive. Some investigators have postulated 14 theoretically possible combinations of defects. It thus has become necessary to use a more comprehensive title to encompass all variants of this expanded group of lesions. The term "endocardial cushion defects," previously proposed by Watkins and Gross, seems appropriate for this purpose, since the basic abnormality common to each of the variants results from defective development of the endocardial cushions.

The case records of all patients in whom cardiac defects of this type were found at open-heart operations performed at the Mayo Clinic have been reviewed. There were 54 such patients, the first having been operated on in March, 1955, and the others between that date and Jan. 1, 1959. From a practical clinical standpoint, it seemed best to classify endocardial cushion defects into 4 groups. There is no objection to the anatomic classification of certain defects in a transitional or intermediate group between the partial and the complete form of the common atrioventricular canal; however, these transitional varieties typically function as either partial or complete forms of the defect, and hence it has seemed impractical in this study of surgical patients to attempt to separate such intermediate forms.

Included in the group of 54 patients are examples of the 4 varieties of endocardial cushion defects, namely, partial atrioventricular canal, complete atrioventricular canal, ventricular septal defect with cleft atrioventricular valves, and common atrium. A marked difference was apparent between the partial and the complete form of this defect, both in the natural history and in the results of surgical treatment. For the partial form, surgical repair was highly successful and safe, even to a degree comparable to the repair of the ordinary atrial septal defect. For the complete form, operative mortality was very high. The 2 examples of ventricular septal defect with cleft atrioventricular valves are believed to be the first of this type which have been reported. Certain techniques and principles for the repair of these lesions have become apparent during this experience. Of particular importance is the requirement that the function of the atrioventricular valves be restored by the repair to as nearly normal as is possible.

Treatment of Esophageal Varices by Partial Esophagogastrectomy and Interposed Jejunal Segment. D. V. Habif. Surgery 46:212-237 (July) 1959 [St. Louis].

This report deals with the author's experience in trying to achieve a permanent cure from varix hemorrhage for patients who cannot have a portacaval shunt, and the present plan of operative treatment evolved from this experience. From August, 1948, through July, 1951, 7 patients were operated on. The operation was an almost total gastrectomy, leaving 2 cm. of stomach on the greater and lesser curvature sides below the esophagogastric junction. Two patients have had no bleeding to date, but 5 had subsequent bleeding and 3 of these had a successful lower one-third esophagectomy. From December, 1952, through October, 1958, 21 patients were operated on. The operation was a partial esophagogastrectomy of the lower third of the esophagus and the upper 5 cm. of stomach. Seventeen patients had extrahepatic block, and 4 had cirrhosis. There were 4 deaths, and among the 17 survivors, 2 had further hemorrhage. Nineteen of the 21 patients had reconstruction with an interposed isolated segment of jejunum—7 with an isolated vascular pedicle where the intestine was supplied through a single artery and vein to the arcuate, and 12 without interruption of the arcuate vessels distally.

The following plan of treatment has been evolved for the nonemergency definite treatment of patients with portal hypertension and recurrent bleeding from esophageal varices: (1) a portacaval shunt of some type; (2) transesophageal ligation of varices for children under the age of 7 or 8 years, who have frequent episodes of hematemesis and have an intact spleen where the splenic vein is as yet too small for a splenorenal shunt and no other shunt is possible or successful; it is a temporary measure, however, since a splenorenal shunt may be attempted at a later date; (3) partial esophagogastrectomy with interposition of a jejunal segment for patients who are "shunt failures" or cannot have a shunt; and (4) resection of the midesophagus for those patients who have bleeding from residual varices after lower one-third esophagectomy.

Metastases of the Internal Mammary Chain of Lymph Nodes in Patients with Mammary Carcinoma. G. Silini and P. Metalli. Minerva chir. 14:455-464 (May 15) 1959 (In Italian) [Turin, Italy].

The internal mammary chain of lymph nodes was early involved in the metastatic process of mammary carcinoma in 25 patients who underwent the classical radical operation on the breast and clearing of the homolateral parasternal region. Microscopic examination of the removed material revealed involvement of the internal mammary chain of lymph nodes in 10 patients (40%) and of the axillary lymph nodes in 21 (84%). The axillary lymph nodes were involved in all instances in which there was metastasis of the internal mammary chain of lymph nodes. If metastases of the axillary lymph nodes were not present, the internal mammary chain of lymph nodes was not involved either. The size of the primary lesion was about 3.3 cm. in diameter if the axillary lymph nodes were involved and was under 2 cm. if they were not involved. The size of the primary lesion was about 3.6 cm. in diameter if the internal mammary chain of lymph nodes was involved and it was about 2.7 cm. if it was not involved. Of 10 instances of metastases of the internal mammary chain of lymph nodes, 6 were adenocarcinomas; 2, hard carcinomas; 1, scirrhous carcinoma; and 1, vegetating carcinoma. The same varieties of carcinoma were found in the metastatic material obtained from the axillary region. Malignant epithelial cells were found in lymphatic tissue around the arterial vessels in 2 patients after they had been cleared for involvement of the internal mammary chain of lymph nodes. This incidence suggests the necessity of a thorough inspection of the vascular fasciae between the lymph nodes before making the diagnosis of noninvolvement of the adjacent areas.

From the early invasion of the internal mammary chain of lymph nodes, it could be interpreted that there exists a certain relationship between the stage of the neoplastic disease and the involvement of the internal mammary chain. Nothing can be said about a possible correlation between the location of the primary lesion and the histological variety and frequency of metastases in the peristernal region.

Single or Double Segments of the Lung Occupying a Hemithorax: Clinical and Physiologic Evaluation. R. H. Overholt, E. A. Gaensler and J. A. Bougas. New England J. Med. 261:10-18 (July 2) 1959 [Boston].

Disease may destroy all but 1 or 2 segments of a lung. Often surgery is imperative, with a choice between pneumonectomy and conservation of the single or double segment. If there is disease on the opposite side, preservation of functioning lung tissue becomes important. Although lobectomy combined with segmental resection theoretically provides maximal preservation of function, it may present more formidable technical problems and postoperative hazards than pneumonectomy. Such added effort and risk can be justified only if it can be shown that the 1 or 2 residual segments contribute significantly toward the pulmonary economy. Because no data are available from the literature concerning clinical course and pulmonary function with single-segment or double-segment occupancy in a hemithorax, a late postoperative study of such patients was made. On 14 occasions during the past 12 years the opportunity presented for studying patients with 1 or 2 segments remaining within a hemithorax. All had undergone extensive pulmonary resection on one or both sides for treatment of severe bronchiectasis that had produced disabling symptoms.

Clinical and physiological data obtained in studies on these patients leave no doubt that, in most cases, 1 or 2 healthy residual segments on one side may contribute greatly to over-all functional capacity. In patients with intact and presumably healthy opposite lungs, preservation of 1 or 2 segments resulted in greater over-all function than is ever seen after pneumonectomy. A single segment was found to contribute as much as 23%, and 2 segments as much as 33% to total oxygen uptake at rest. In addition, the residual lung tissue prevented, or greatly reduced, mediastinal shift to the side of operation. With contralateral inoperable bronchiectasis, the share of function of the remaining segments did not increase as expected, presumably because they also were involved by disease, which was diffuse throughout all parts of the lung. After extensive contralateral resection the 1 or 2 remaining segments made a larger contribution to the greatly taxed respiratory economy and, in extreme cases, were responsible for nearly half the total respiratory work. In nearly all cases with functioning residual segments, their ventilatory contribution was relatively greater than their participation in oxygen uptake. This unfavorable ventilation-perfusion ratio may have been disturbing in one case. The functional contribution of the single and double segments in patients with well opposite lungs was greater than that predicted from theoretical consideration. In 4 cases with extensive disease or resection on the opposite side, the residual lung tissue was probably necessary for life.

Traumatic Mediastinitis and Thrombosis of the Superior Vena Cava. J. E. Rodo. Medicina 19:17-27 (Feb.) 1959 (In Spanish) [Buenos Aires].

Thrombosis of the superior vena cava, due to mediastinitis from direct trauma, is rare. The signs and symptoms depend on the velocity at which obstruction of the superior vena cava has taken place and the acuteness of the obstruction. The characteristic signs and symptoms are: (1) edema and cyanosis of the face, neck, arms, and hands (which increase when the patient is lying down and diminish in the standing position); (2) venous hypertension in the arms and normal venous tension in the legs; (3) development of varicose veins in the anterior and lateral surfaces of the thorax; and (4) establishment of deep collateral venous circulation and dyspnea. The treatment consists of thoracotomy with removal of cicatricial tissue for liberation of the newly formed collateral vessels.

A 32-year-old man reported for consultation with typical signs and symptoms of obstruction of the superior vena cava one year after the occurrence of trauma to the chest. The results of phlebographies confirmed the clinical diagnosis of caval obstruction. The operation consisted of median sternotomy and removal of fibrous tissue for liberation of the superior vena cava. Histological examination of the removed tissue showed chronic inflammation. The postoperative period was uneventful, and the patient was discharged in a satisfactory condition. A follow-up for 6 years has shown that he has been in normal health since the operation. The roentgenograms of the chest have been normal. Moreover, the venous hypertension in the arms has diminished (in comparison with the condition before the operation); this fact is probably due to improvement of the collateral circulation after the operation.

Results of the Treatment of Postoperative Peptic Ulcer by Vagotomy. L. Ruyters, P. Maquet and F. Orban. Acta gastro-enterol. Belg. 22:187-211 (April) 1959 (In French) [Brussels].

The authors present the results obtained by transthoracic bilateral vagotomy in 14 patients with postoperative peptic ulcer. The original operation consisted of gastrectomy in 11 cases and of gastrojejunostomy in the other 3. The period of follow-up after vagotomy ranged from 5 months to 6½ years.

All the patients presented symptoms suggesting ulcer: epigastric or left hypochondriac pain, in rhythm with meals and relieved by alkalines at first but later becoming severe and unresponsive to the ingestion of food or alkalines; significant gastric hemorrhage at times; undernourishment due to fear of pain or anorexia; and inability to work normally.

The results of vagotomy were excellent in 8 patients with peptic ulcer following gastrectomy: clinical improvement was accompanied, first, by a reduction in, and, later, by the disappearance of, the roentgenologic picture of ulcer. Good but less perfect results were obtained in the patients with gastrojejunitis and hyperacidity; one continued to have mild dyspepsia of a gastritic type, and all showed hyperacidity in the fasting state. The standard procedure in the patients who had undergone gastroenterostomy would have been a degastrogastrectomy. Two of them, however, were so old that their ability to withstand such a serious operation was uncertain. Vagotomy was, therefore, given a trial and was followed in each case by clinical and radiologic cure. The third patient in this group had an extremely large ulcer niche, and vagotomy was decided on as a first step to reduce inflammatory phenomena. The results were so satisfactory that no further operation was needed, and the patient has remained well for 6 years.

Vagotomy thus appears to be an excellent procedure for patients with postoperative peptic ulcer. It entails a minimum of operative risk and may produce a complete cure. It is not an absolute safeguard against recurrence, but the same may be said of reoperations on the stomach, which are not always effective and which may lead to total gastrectomy.

NEUROLOGY & PSYCHIATRY

Cerebral Paragonimiasis: A Report of Forty-Seven Cases. S. K. Kim. A. M. A. Arch. Neurol. 1:30-37 (July) 1959 [Chicago].

The habit of eating raw crabs and other crustaceans is responsible for infection by the lung fluke, Paragonimus westermani. This habit is prevalent in Far Eastern countries, where paragonimiasis is endemic. Since Otani, of Japan, first called attention to the high incidence of cerebral involvement in 1887, there have been many case reports based on postmortem examination, but only 21 instances of cerebral paragonimiasis have been demonstrated surgically. The present paper is based upon the cases of 47 persons examined by the author; the diagnosis was made at the time of operation in 45 cases and at autopsy in 2. Almost all the patients gave a history of eating raw and poorly cooked crab and/or crayfish. Some apparently were infected through raw fish or impure water.

By far the commonest initial manifestation of cerebral paragonimiasis was a seizure (31 cases). The remainder of the patients, with 2 exceptions, had a seizure at some time in their course. The type of seizure seemed to depend upon the localization of the intracranial lesion. The majority of the patients gave a history of some type of paroxysmal minor impairment of neurological function, which after a time developed into frank grand mal attacks. Patients with multiple cysts frequently had several types of convulsive episodes. Sudden hemiplegia was the first symptom in 6 patients. In 6 other patients the predominant symptoms were those of chronic meningitis, with headache, stiff neck, vomiting, and fever. Severe headache associated with papilledema was noted in 7 patients, but others complained of mild headache. Fever was noted in 8 patients. Feeblemindedness was frequent.

The diagnosis of cerebral paragonimiasis is usually suggested by hemoptysis in a young person (generally a peasant) who lives in an Oriental country where the disease is endemic and who has had some mental impairment and symptoms of cerebral involvement, such as convulsions or a stroke. The finding of ova or a fluke in the sputum or stool would confirm the diagnosis; the complement-fixation test might help. Eosinophilia in the blood is suggestive of paragonimiasis in an Oriental. Roentgenograms of the skull and chest usually show typical lesions. In treatment, emetine and antimony sodium tartrate (Stibnal) were given to 9 patients in this series, and resulted in a discharge of ruptured ova in the sputum. The cerebral symptoms were not improved.

The author lists criteria favoring the presence of a localized process suitable for surgical excision, as well as criteria indicating multiple or diffuse lesions not suitable for surgical treatment. Surgical resection of the cerebral abscess often relieved the convulsive episodes, although some patients continued to have less frequent minor seizures. If the brain abscess was not surgically removed, even though it became calcified or well encapsulated, generalized seizures persisted for long periods. While in patients with localized lesions surgical excision offers a good chance for relief of the epilepsy and arrest of the cerebral disease, in those with diffuse and multiple lesions surgery has little to offer.

Cerebral Vasospasm in Angiography for Intracranial Aneurysms: Incidence and Significance in One Hundred Consecutive Angiograms. T. M. Fletcher, J. M. Taveras and J. L. Pool. A. M. A. Arch. Neurol. 1:38-47 (July) 1959 [Chicago].

This study is concerned with the clinical implications of cerebral vasospasm as determined by angiography. The authors believe that spasm of the internal carotid artery or its major branches is a common accompaniment of ruptured intracranial aneurysm and that the patient's clinical course may be dependent to a large degree upon the presence, extent, and duration of this spasm. It may result in localized or generalized insufficiency of the cerebral circulation, thereby producing ischemia of varying degrees in the involved areas of distribution. Recognition of the occurrence of the spasm may be of considerable value to the neurologist and the neurosurgeon alike, particularly as to prognosis and as a guide to management, and occasionally in diagnosis or localization. The authors designate as spasm a narrowing of the lumen of a vessel beyond what they consider a normal anatomic variant.

Up to 1957 it was the policy at the Neurological Institute of New York to carry out angiography after the patient's clinical condition had become stable and there were no signs of continued or new bleeding. In only one-tenth of the patients in this series was angiography carried out before the 5th day. It was not thought that angiography altered the course of the disease except in 4 cases, in which the patient's condition became worse after the procedure, and only 2 of these demonstrated spasm. Angiography was performed by means of percutaneous puncture of the common carotid artery, and serial films were made by identical roentgenologic techniques. For the purposes of this study the cerebral angiograms of 100 consecutive patients with intracranial aneurysm were reviewed and correlated with the clinical history, findings, and course. Cerebral vasospasm did not occur in major cerebral arteries having clear-cut evidence of arteriosclerotic changes, presumably because such vessels are no longer capable of spasm. The type of vasospasm under discussion usually occurred within 3 weeks of aneurysmal rupture and was usually associated with bloody cerebrospinal fluid.

Recognition of the presence of vasospasm is of particular value as a guide to prognosis and management, and occasionally is of localizing value when an aneurysm fails to fill with contrast material or when multiple aneurysms are present. The presence of gross blood as a local irritant is one explanation for the production of spasm. However, since spasm may occur in the absence of blood, and is usually absent on the opposite side from a bleeding aneurysm, there may be an additional factor in the production and maintenance of cerebral vasospasm. This could be a local muscle or nerve reflex effect caused by the distention or rupture of the aneurysm. The occurrence of vasospasm and serious resultant neurological signs may be delayed for several days after subarachnoid hemorrhage, indicating the advisability of prompt surgical treatment of ruptured intracranial aneurysms.

Chlorpromazine—Four Years Later. W. Tuteur, R. Stiller and J. Glotzer. Illinois M. J. 116:9-12 (July) 1959 [Chicago].

The authors report on a 4-year continued survey of 822 psychiatric female patients treated with chlorpromazine. The patients, the largest age sector of whom was between 41 and 50 years, presented symptoms of incontinence, combativeness, destructiveness, noisiness, and tendency to undress; the majority of them had been hospitalized for from 1 to 15 years. Seventy-seven of the 258 patients who were conditionally discharged during the 4-year period, to be followed by systematic treatment with chlorpromazine, have returned, 26 of them for relapses which occurred while taking the drug diligently. The doses of chlorpromazine given to inpatients ranged from 100 to 1,200 mg. orally, or 50 to 150 mg. intramuscularly, per day; doses for outpatients varied from 50 to 800 mg. orally. During the 4-year survey 6 patients out of a total of 181 discharged patients have been away from the institution for more than 3½ years, 36 for 3 to 3½ years, 24 for 31 to 36 months, and 34 for more than 2 years. Fifty-five of the 181 patients remaining outside the institution have found gainful employment. Placebos were given to 72 discharged patients, and 43 suffered from relapses, showing symptoms similar to their pretreatment clinical picture and indicating that they might need drug treatment for an indefinite time. Five of these had to be rehospitalized, but the others showed sufficient improvement within several days after treatment with chlorpromazine had been restarted.

The authors point out that since the introduction of chlorpromazine it has been possible to remove 118 beds from the overcrowded cottages of the institution where the study was made. These same cottages used to discharge only 2 to 6 patients a year before the introduction of this beneficial drug.

Virus Infections of the Central Nervous System Transmitted by Arthropods in Europe. H. Moritsch. Schweiz. med. Wchnschr. 89:683-685 (June 27) 1959 (In German) [Basel, Switzerland].

Among the epidemic virus diseases transmitted by arthropods, such as western equine encephalomyelitis and hemorrhagic or Q fever, spring-meningoencephalitis represents the most important infection of the central nervous system in Europe. Of the 162 patients with virus infections of the central nervous system, who were admitted between 1956 and 1958 to the Neunkirchen (Austria) Hospital, 89 (55%) had spring-meningoencephalitis. The onset of the disease is similar to that of poliomyelitis. Clinically, this virus infection can be divided into 3 forms: meningitis, meningoencephalitis, and paralytic meningoencephalitis. A particular characteristic of the latter form is the late appearance of paralysis which, despite a marked initial atrophy, has a tendency to complete regression. There is no specific treatment for spring-meningoencephalitis, any more than there is for poliomyelitis. In general, the course of the disease is mild. Among the 89 patients with spring-meningoencephalitis reported, only 5 (5.6%) died.

It is difficult to differentiate spring-meningoencephalitis due to virus infection from poliomyelitis by the anatomicopathological aspects of the central nervous system alone. The etiology of the disease can only be diagnosed correctly by means of serologic and virologic examinations. The importance of systematic laboratory investigations in all diseases of the central nervous system caused by virus infection is emphasized.

Polyarteritis Nodosa and the Nervous System. K. Koppang. Tidsskr. norske laegefor. 79:679-683 (June 1) 1959 (In Norwegian) [Oslo].

Polyarteritis nodosa occurs more frequently than was previously believed. The nervous system is affected in about half of the cases. The predominating neurological symptom is polyneuritis, often with asymmetrical involvement. Symptoms from the central nervous system are less frequent. The possibility of polyarteritis nodosa should be considered in polyneuritis accompanied by fever, increased sedimentation reaction, and simultaneous symptoms from other organs. Positive biopsy findings are not necessary to establish the diagnosis in life. If polyarteritis nodosa is suspected, careful search for possible allergens, especially medicaments, is called for. The course of the disease can to some extent be influenced by cortisone treatment.

GYNECOLOGY & OBSTETRICS

A Study of the Aetiological Factors in Carcinoma of the Cervix Uteri in Guntur. P. S. Rao, R. S. Reddy and D. J. Reddy. J. Indian M. A. 32:463-470 (June 16) 1959 [Calcutta].

The authors report on 758 patients with symptoms pointing to lesions of the uterine cervix, who were screened at the gynecologic outpatient clinic of the General Hospital in Guntur, India, between December, 1957, and February, 1959. To evaluate the relative incidence of carcinoma of the uterine cervix among different religious groups, patients of the same age-group attending the same hospital during the same period for diseases other than carcinoma of the cervix were grouped according to religion and served as contratest patients. All cases of carcinoma of the cervix were histologically confirmed except 30 cases.

Findings suggest that there is a definite relationship between the incidence of carcinoma of the cervix and the different religious groups. A high incidence of carcinoma of the cervix was observed among the Hindus and Christians whose partners were uncircumcised. The male partners of these patients showed higher grades of smegma accumulation. Carcinoma of the cervix was significantly low among the Moslems. No case of carcinoma of the penis was encountered among Moslem patients during the period of investigation. This emphasizes the causal role of smegma in carcinoma of the cervix. The peak incidence of carcinoma of the cervix was observed in patients between 31 and 50 years of age and in those who were in the premenopausal stage of life. The majority of the patients with carcinoma of the cervix belonged to the lower income groups.

Twenty out of 475 biopsy specimens obtained from patients with carcinoma of the cervix showed a definite association between chronic cervicitis and carcinoma of the cervix. Transition between cervicitis and neoplastic change could be demonstrated in every one of these 20 cases. It is pointed out that the recent experimental production of carcinoma of the cervix in mice by horse and human smegma should be evidence enough to frighten Americans to resort to mass circumcision of newborn male infants.

The Influence of Certain Etiological Factors in the Appearance of Cancer of the Cervix Uteri and of the Breast. C. Gros, R. Keiling and R. Renaud. Semaine hôp. Paris 35:1968-1973 (June 12) 1959 (In French) [Paris].

At the Anticancer Center and Faculty of Medicine of the University of Strasbourg the authors studied the influence of race, marital status, and pregnancy on the frequency of cancer of the cervix uteri and of the breast. Out of 512 cancers of the cervix, 4 were in Jewesses, and among 724 cancers of the breast, 34 were in Jewesses. Cancer of the breast appeared significantly more frequently in Jewesses than in non-Jewesses, and cancer of the cervix appeared much less frequently in Jewish than in non-Jewish women. An attempt is made to explain the latter fact through hygienic conditions which would account for the presence of less preputial smegma, a substance which was demonstrated by Plaut and Khon Speyer to be cancerogenic. An ethnic explanation is that the Jews have a marked degree of consanguinity, and a genetic factor may be responsible for resistance of the cervix uteri to cancerogenic substances.

Marital status appears to play an important role in the relative frequency of these 2 cancers. Both cancer of the cervix uteri and cancer of the breast appear more frequently in married than in unmarried women, but this difference between the married and the unmarried is less marked in cases of cancer of the breast. The authors' percentages tally absolutely with those given by other investigators in different countries. In attempting to define the influence of pregnancy, the authors found that there was a higher proportion of sterile married women with epithelioma of the breast than with epithelioma of the cervix. The frequency of cervical cancer increases rapidly with the number of pregnancies. Cancer of the cervix uteri is less frequent than cancer of the breast in women with 1 or 2 pregnancies, but it surpasses the frequency of cancer of the breast when there have been more than 2 pregnancies. The authors' statistics are in complete agreement with those of other cancerologists on this point. Lastly, they cite the fact that study by other investigators of the menstrual cycle, of the age at marriage and first pregnancy, and of the number of pregnancies shows much genitohormonal activity in women afflicted with cancer of the cervix uteri. The question is raised as to whether estrogens play a large part in the appearance of this cancer.

Effects of 17α-Methyl-19-Nortestosterone in Pregnancy and in Threatened Abortion. A. Foix, R. O. Bruno and J. Carpinacci. Obst. y ginec. latino-am. 17:229-235 (March-April) 1959 (In Spanish) [Buenos Aires].

The synthetic nor-steroid, 17α-methyl-19-nortestosterone (or methyl-estrenolone), has a marked progestational action with only a mild androgenic effect. It has, therefore, a wide field of application in gynecology. The authors studied its effects in 2 groups of patients. The first group was composed of 10 pregnant women, between the ages of 22 and 38 years, with pregnancies of 40 to 60 days, who had had spontaneous abortions or had become pregnant after treatment for sterility. Six had had at least one abortion; one had had 3 abortions. As a criterion for the administration and dosage of 17α-methyl-19-nortestosterone, special attention was given to the changes in the vaginal cytology. The treatment was started as soon as the index of acidophilic karyopyknic cells exceeded 20%. The initial dose was 2 to 5 mg. daily. Four days later the cytological test was repeated, and the dose was maintained, increased, or decreased according to the findings. This procedure was followed as long as the cytological conditions indicated the need for medication. In 6 patients the pregnancy was following a normal course when this article was written; 2 patients had normal deliveries at term; one had an abortion (probably due to torsion of the umbilical cord); and in one the treatment had to be discontinued because of intolerance symptoms, although the vaginal cytology had improved during the period of medication tolerance.

The second group was composed of 21 patients, between the ages of 23 and 32 years, who showed symptoms of impending abortion. Eight patients had metrorrhagia, 2 had pain, and 2 had both metrorrhagia and pain. Fifteen patients had had one or more spontaneous abortions. The pregnancy stage varied from 1 to 5 months. The doses of 17α-methyl-19-nortestosterone administered to these patients were higher than those administered to the patients in the first group. In some cases they reached 15 mg. daily until the symptoms of impending abortion had abated or disappeared. The treatment was then continued with smaller doses until normalization of the vaginal cytology was achieved. In 10 patients the pregnancy was following a normal course when this article was written; one had a normal delivery at term; 8 had abortions; and in 2 cases the results were unknown. Taking both groups as a whole, one-third of the patients had edema of the face and other signs of intolerance to the drug. The authors believe that the likelihood and severity of intolerance will be greatly reduced by administering 17α-methyl-19-nortestosterone by the sublingual route instead of the alimentary route used in this study. The results are termed encouraging, especially when one considers that all the patients studied had a manifest tendency to interruption of the pregnancy.

PEDIATRICS

Association of Type 2 Hemadsorption (Parainfluenza 1) Virus and Asian Influenza A Virus with Infectious Croup. A. J. Vargosko, R. M. Chanock, R. J. Huebner and others. New England J. Med. 261:1-9 (July 2) 1959 [Boston].

In the fall of 1957 a study to isolate new viruses and to associate these agents with clinical illness, including croup, was initiated by the virus section, Research Foundation of the Children's Hospital of the District of Columbia, and the laboratory of infectious diseases, National Institutes of Health. The 47 patients who are the subjects of this report were admitted to the Children's Hospital of the District of Columbia because of an acute croup syndrome during the year from October, 1957, through September, 1958. Specimens were collected during the same interval from 949 infants and children who were free of respiratory-tract illness. Those included hospital patients during the entire study period and children from the "well-child" and outpatient clinics. The mean age for the patients with croup was 24.7 months; that for the patients without respiratory disease was 24.6 months. Oropharyngeal swab specimens and serums taken from the latter patients were treated in the same manner as those from patients showing clinical respiratory illness.

Viral agents were recovered from 16 (or 34%) of the patients with croup. Hemadsorption virus type 2, which was recovered from 12 (or 25%) of the patients with croup, was the agent most frequently encountered. Hemadsorption virus type 1, croup-associated virus, adenovirus type 1, and adenovirus type 5 were each isolated once. The association of hemadsorption virus type 2 with croup appears to be significant. The recovery of this agent from infants and children without respiratory-tract illness occurred at a rate of only 0.2%.

From the serologic data obtained in this study, a diagnosis of viral infection could be assigned to 71% of the children with croup. The viruses associated included influenza virus, hemadsorption virus types 1 and 2, croup-associated virus, and adenovirus types 1 and 5. The agents whose association with croup was best substantiated were hemadsorption virus type 2 and the virus of Asian influenza type A, both myxoviruses. The Asian influenza virus was associated with 5 (36%) of 14 croup illnesses during the month when that agent was most prevalent, and in 19% throughout the year. Infection with type 2 hemadsorption virus was associated with 17 (36%) of 47 patients with croup seen throughout the year. Evidence for infection with Asian influenza virus or hemadsorption virus type 2 was found in approximately 55% of all the croup patients studied. Infection with type 2 hemadsorption virus was found predominantly in boys, but its clinical features were not distinctive. In an addendum it is stated that the high level of association of hemadsorption virus type 2 with the croup syndrome described in this paper was maintained from October, 1958, through May, 1959. Hemadsorption virus type 2 was recovered from 7 (16%) of the 44 patients studied during this interval. Additional evidence for the role of hemadsorption virus type 1 in the croup syndrome was the isolation of this agent from 3 of the 44 patients.

The association of Asian influenza with croup is not surprising to clinicians, who have believed for years that influenza viruses may cause croup. The association of hemadsorption virus type 2 with croup is the most striking finding in the studies on hemadsorption viruses. These agents are new myxoviruses that will shortly be classified as Myxovirus parainfluenzae 3 (hemadsorption virus type 1) and Myxovirus parainfluenzae 1 (hemadsorption virus type 2).

Tuberculous Lesions in Children Who Have Been Inoculated with the BCG Vaccine: Observations in 56 Children Seen at a Sanatorium. N. Ebers, Tuberkulosearzt 13:397-399 (June) 1959 (In German) [Stuttgart, Germany].

A study of 56 children shows that a diagnosis of active tuberculosis is made much too often not only in children in general but in those who have been vaccinated. The 56 children studied had been inoculated with the BCG vaccine. They were admitted to the Elisabethenberg Sanatorium, in Germany, between 1948 and 1958 with a diagnosis of "active tuberculosis." Detailed examination of these children revealed an active process in only 13 cases, and only 5 of the cases were attributable to genuine failure of the BCG vaccine to confer protection. The number of BCG-inoculated children who subsequently developed active tuberculosis was an exceedingly small fraction of the total number of tuberculous children who were admitted to the sanatorium during the same period.

Neonatal Thyrotoxicosis. S. N. Javett, B. Senior and S. Heymann. Pediatrics 24:65-73 (July) 1959 [Springfield, Ill.].

The authors report on 2 cases of neonatal thyrotoxic exophthalmic goiter in infants born of mothers with exophthalmos and inadequately controlled thyrotoxicosis. The mothers, who had received treatment before conception with radioiodine (I^{131}) and thyroidectomy, were at the time of delivery not only thyrotoxic but markedly exophthalmic. The infants were desperately ill at birth with a state resembling thyroid storm. Intravenous and oral administration of Lugol's solution proved lifesaving. Medication was required for 4 or 5 weeks, the patients remaining well thereafter. Appraisal of the pathogenesis of neonatal thyrotoxicosis favors the transplacental passage of a thyroid-stimulating agent, probably derived from the mother's pituitary. The thyroid status of neonates born of mothers taking medication for thyrotoxicosis reflects the interaction between the transmitted thyroid-stimulating agent and the particular drug being employed.

Ectasia of the Coronary Vessels in the Course of Periarteritis Nodosa in a Nursling Aged 2½ Months. R. Turpin, L. Becquet, R. Gorin and J. Cruveiller. Semaine hôp. Paris 35:1779-1786 (May 24) 1959 (In French) [Paris].

Periarteritis nodosa is so rare in infants aged less than one year that only about 20 reports are to be found in the literature, and some of these are open to question. The present case, which occurred in an infant, aged 2½ months, was a striking example of the contrast between the commonplace clinical syndrome and the wide diffusion of the ectatic lesions of the arteries of medium and small caliber. The clinical manifestations consisted of acute febrile rhinopharyngitis followed by diarrhea, abdominal meteorism, moderate enlargement of the liver, polynucleosis with eosinophilia (10%), and minimal albuminuria. The child had apparently recovered when death suddenly occurred within a few seconds. Autopsy revealed ectasia of the coronary vessels with involvement of various renal, hepatic, splenic, duodenopancreatic, mesenteric, and appendicular arterioles. The cerebral and pulmonary arteries, on the other hand, were not af-

about two-thirds of the patients, and the endogenous nature in the one-third. The ancestors of the children with bronchial asthma of allergic origin had frequently had diseases of an allergic nature. The preparation from the anterior lobe of the pituitary was administered intramuscularly to the children with bronchial asthma every other day in trimester courses, with a month-long, drug-free interval in between, for a period of 1 or 2 years. At the beginning the doses were small and were gradually increased afterwards. The type of preparation administered was changed several times to prevent the formation of antihormones. No other symptomatic treatment was given. All the patients were cured of bronchial asthma, 31 (78%) of them after the first year and the remainder during the second year of treatment. Inspection of the patients 2 years after the remission of symptoms confirmed the definitive cure of bronchial asthma.

The second group consisted of 65 patients with recurrent urticaria and of 28 patients with atopic dermatitis. Small or medium-sized doses were administered intramuscularly every other day for 2 trimesters, with a drug-free month in between. The relief from symptoms was faster in these patients than in those with bronchial asthma, and there were no sequelae. The first symptom to subside was pruritus. The author believes that the hormonal action of the preparation not only afforded relief from urticaria and eczema but also had an antiallergic effect.

THERAPEUTICS

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The effectiveness of a new xanthine derivative (X-D), Ro 1-8239, was studied in a group of 12 patients suffering from chronic pulmonary obstructive emphysema with cardiovascular involvement (chronic cor pulmonale). In all these patients complete clinical and radiologic examination showed dyspnea, both at rest and during effort, bronchial symptoms, diaphragmatic flattening and hypomobility, and intercostal space dilatation. In 6 patients the emphysema was in an advanced stage; in the other 6 it was of a moderate degree. In all the patients complete spirometric studies, as well as determination of residual air volume and total pulmonary capacity, were performed at rest and 30 minutes after the intravenous administration of 0.1 Gm. of Ro 1-8239. Intracardiac catheterization was performed in 5 patients, with administration of 0.1 to 0.2 Gm. of the X-D into the pulmonary circulation. Three of these 5 patients received a dose of 0.25 to 0.50 Gm. of chloral hydrate as a premedication. All 5 patients were examined within 30 to 60 minutes after the administration of the X-D. Three normal subjects and 15 patients with pulmonary emphysema, treated with aminophylline and dihydroxytheophylline in doses equivalent to the doses of the X-D given to the experimental group, served as a control group regarding the spirometric, ventilation, and arterial blood values. Eight patients with simple mitral stenosis formed the control group in the study of pulmonary circulation by catheterization.

The effects of the X-D were evidenced mainly in the changes observed in pulmonary ventilation and arterial blood. There was a significant reduction in the air spaces and in the ratio of these spaces to the tidal air volume, with a consequent increase in the alveolar ventilation and in the arterial pH. There was also a statistically significant drop in the arterial oxygen content and arterial saturation, which the authors attribute to the changes produced in the ratio of ventilation to perfusion throughout the lungs and/or to increased flow through poorly or nonventilated areas. These results suggest that Ro 1-8239 acts mainly upon small vessels, both pulmonary and systemic.

fected. The integrity of the electrocardiographic tracings contrasted strongly with the intensity of the coronary lesions.

No possible cause, and in particular no therapeutic sensitization, by vaccination or treatment with antibiotics or chemotherapy, could be found for the appearance of periarteritis nodosa in this infant. The histopathological lesions suggested a latent, subacute process, extending over a period of several weeks, if not months, and compensated for during much of the time. This, of course, brings up the problem of a possible intrauterine cause.

Treatment of Disseminated Infantile Histoplasmosis With Amphotericin B. J. Little, J. Bruce, H. Andrews and others. Pediatrics 24:1-5 (July) 1959 [Springfield, Ill.].

The authors report on 3 infants, under the age of 1 year, and a child of 3 years, who were treated for disseminated histoplasmosis with amphotericin B (an antifungal agent derived from an unidentified Streptomyces species found in a South American soil sample). The patients were given amphotericin B intravenously in a daily dosage which varied between 0.25 and 1.0 mg. per kilogram of body weight. The calculated amount of the drug was dissolved in 5% dextrose in water, so that a concentration of 1 mg. of drug per 10 ml. of solution was not exceeded. The rate of infusion was adjusted, so that the dose was given over a 6-hour period. The continuation of medication for 4 to 8 weeks is recommended, but 2 of the patients responded well to shorter courses. Headache, nausea, and vomiting were early toxic manifestations of therapy. Elevations of the level of nonprotein nitrogen in the blood, without other evidence of renal disease, have been observed. Chills, fever, and an anaphylactoid-like reaction with peripheral cyanosis were observed in one infant after the first injection. The use of an antihistamine drug and epinephrine in oil apparently controlled the reaction, so that therapy could be continued. The medications were discontinued after the 12th day of treatment without return of the reactions.

A definite diagnosis of disseminated histoplasmosis is desirable before therapy is started because of the technical difficulties of treatment with amphotericin B. The authors recommend the Heiner agar-gel technique for histoplasmin precipitin reaction as a diagnostic tool. In this technique antigens are prepared from stock cultures of fungi and from cultures freshly isolated from patients, and undiluted serums of patients are used for antibody sources. This test is easy to perform and has greater sensitivity and specificity than other immunological tests. The response of the 4 children in this series to therapy was gratifying. All the patients are doing well, and there is no indication of relapse or exacerbation. The response seems to warrant further trial of amphotericin B in this frequently fatal disease of infancy.

Citric Acid and Rickets: Recent Views on the Calcium-Phosphorus Metabolism. R. Rossi and R. Cremoncini. Minerva pediat. 11:606-615 (May 19) 1959 (In Italian) [Turin, Italy].

A combined preparation of citric acid–calcium-phosphorus was given to a group of 30 infants with rickets and to a control group of 10 healthy infants and children, aged up to 10 years. The control group received a daily dose of 2.2 or 4.4 Gm. of the compound for 10 days. The serum calcium value tended to increase in 8 of the 10 infants and children of the control group after they had received the preparation, but it became normalized 10 days after the administration of the last dose. Phosphatemia and the concentration of phosphorus in the serum either increased or decreased as a result of the therapy.

Of the 30 infants with rickets, who ranged in age from 4 to 15 months, 3 had a moderately severe variety and 27 a mild variety of the disease. Among the latter group, 10 had previously received treatment with prophylactic dosages of vitamin D, 9 had previously received treatment with therapeutic dosages of vitamin D, and 8 had not previously received any treatment with vitamin D. The treatment with the combined preparation of citric acid-calcium–phosphorus lasted 2 months and consisted of daily doses of 700 mg. to the infants under 6 months of age, of a double dose to the infants under one year, and of a triple dose to older ones. Two therapeutic doses of vitamin D were administered intramuscularly to 5 patients who had previously received only the prophylactic dose of vitamin D and to 4 infants who had not previously received vitamin D. This treatment produced marked improvement in patients with the mild variety of the disease; it induced increase of the serum calcium value in 17 patients and a normalization of the phosphatemia and of the concentration of phosphorus in the serum in most patients. The treatment produced a fair improvement in patients with the moderately severe variety of the disease.

Hormonotherapy with an Anterior Pituitary Preparation for Bronchial Asthma and Certain Infantile Allergic Skin Disorders. P. Perrotta. Minerva pediat. 11:616-621 (May 19) 1959 (In Italian) [Turin, Italy].

Hormonotherapy with an anterior pituitary preparation was instituted in 40 children, under the age of 12 years, with bronchial asthma and in 93 children, aged between 2 and 8 years, with recurrent urticaria or atopic dermatitis. The allergic nature of the bronchial asthma was presumed in about two-thirds of the patients, and the endogenous nature in the one-third. The ancestors of the children with bronchial asthma of allergic origin had frequently had diseases of an allergic nature. The preparation from the anterior lobe of the pituitary was administered intramuscularly to the children with bronchial asthma every other day in trimester courses, with a month-long, drug-free interval in between, for a period of 1 or 2 years. At the beginning the doses were small and were gradually increased afterwards. The type of preparation administered was changed several times to prevent the formation of antihormones. No other symptomatic treatment was given. All the patients were cured of bronchial asthma, 31 (78%) of them after the first year and the remainder during the second year of treatment. Inspection of the patients 2 years after the remission of symptoms confirmed the definitive cure of bronchial asthma.

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Methimazole and Carbimazole in Hyperthyroidism: A Comparison by a Double Blind Technique. T. H. McGavack. Am. J. M. Sc. 238:1-12 (July) 1959 [Philadelphia].

In 1949 Stanley and Astwood called attention to the highly suppressive influence of certain imidazoles on the uptake of iodine by the human thyroid gland. They were particularly impressed with the usefulness of methimazole (1-methyl-2-mercaptoimidazole) in suppressing radioiodine (I^{131}) uptake and controlling the manifestations of thyrotoxicosis. More recently Lawson, Rimington, and Searle have suggested that the imidazole action could be prolonged by the substitution of a carbethoxy group for the hydrogen of the mercapto group on carbon atom 2 of methimazole. In clinical trial, this compound, carbimazole, has proved about as effective, weight for weight, as methimazole in the management of thyrotoxicosis. From clinical reports, which cover considerably more than 1,000 patients in the case of each drug, carbimazole seems to have produced fewer severe toxic reactions (granulocytopenic and urticarial-febrile reactions) than methimazole.

In view of the claims made for carbimazole, it was decided to have a single group of workers test the activity of each drug without knowing the identity of either, and to make such tests on a weight-for-weight basis. The 2 drugs, identified only by code numbers, have been administered to 123 patients in a series of 203 trials. Methimazole was given initially to 68 patients, and carbimazole initially to 55 patients. The 2 preparations appeared to be equally effective, on a weight-for-weight basis, in controlling the manifestations of hyperthyroidism. Eight toxic reactions were encountered during the administration of methimazole, and 6 with carbimazole. Two of these in association with the use of methimazole were urticarial-febrile reactions. All remaining reactions were manifested by one, or a combination, of the following features: pruritus, localized rashes, and transient edema. It is concluded that both methimazole and carbimazole are effective thyroid blocking agents of approximately equal activity. Methimazole may be more toxic than carbimazole, but a good many more cases should be studied before a hard-and-fast conclusion is drawn regarding this statement, as the differences in the present study are not statistically significant.

Kanamycin. S. M. Finegold. A. M. A. Arch. Int. Med. 104:15-28 (July) 1959 [Chicago].

Kanamycin is a new bactericidal antibiotic which has been shown to be highly effective when given parenterally in the treatment of a number of resistant staphylococcic and gram-negative bacillary infections. The author reviews the literature concerning the use of kanamycin in man and in experimental animals. Used orally, it exerts a profound effect on the normal aerobic intestinal flora, and it has been effective, or has shown promise, in the treatment of some intestinal infections and carrier states. Kanamycin has been adminstered by a variety of routes other than the oral and intramuscular with good results. It has also been used topically or as an irrigating fluid in superficial lesions and wounds and has been applied as an ointment or as a cream. There was no evidence of irritation or of allergic reactions, and the results were generally good.

Toxicity inherent in the drug can be avoided or minimized with careful management. The most important type of toxicity noted with parenteral kanamycin therapy was damage to the 8th nerve, involving both auditory and vestibular functions but chiefly the auditory. Permanent auditory damage may be avoided by stopping the treatment on the appearance of tinnitus. So far there has been little evidence of progression of damage for long periods after the drug has been withdrawn. Care should be exercised in the treatment of elderly patients, because they are more subject to nephrotoxicity and sometimes develop relatively high serum creatinine values. Suggestions as to dosage, precautions to be observed in administering kanamycin, and factors predisposing to toxicity are described in detail.

Statistical Study of the Treatment of Acute Icterogenic Hepatitis with Deltahydrocortisone. P. Mainguet and J. Caroli. Semaine hôp. Paris 35:1974-1986 (June 12) 1959 (In French) [Paris].

The value of deltahydrocortisone (or prednisolone) in the treatment of acute icterogenic hepatitis was investigated by comparing the results obtained in 2 series of patients, one containing 90 patients treated with deltahydrocortisone and the other containing 60 patients treated with standard forms of therapy. The study showed that deltahydrocortisone was incomparably more effective than any of the older methods of treatment when given early in the course of the disease. Progression of the jaundice was checked, regardless of its intensity at the outset, if the patients were given deltahydrocortisone within the first week. No such result was obtained by any of the standard methods of treatment. The therapeutic effect of deltahydrocortisone was also favorable when it was given in the second or the third week of jaundice, but the results had less probative value because it could not be said that spontaneous clearing of the jaundice would have taken much longer.

Various authorities have questioned the value of corticotherapy, saying that the clearing of the jaundice and the improvement in the patient's general condition are misleading and that the corticotherapy has no effect on the biological and anatomic disorders due to the hepatitis. These contentions are disproved by the results obtained in this study, which showed that deltahydrocortisone, when given early, not only cleared the jaundice and produced diuresis, but also led to the return of normal findings in the metabolic tests.

Corticotherapy is less effective and more dangerous when icterogenic hepatitis is prolonged or not promptly treated. Standard methods of therapy, particularly repeated duodenal intubations and cholecystostomy followed by transvesical drainage, retain their full value in such cases. The complications of corticotherapy must be kept in mind, and certain elementary precautions should always be taken. These include routine radiographic studies for the detection of gastric or duodenal ulcer (in suspicious cases) and of pulmonary tuberculosis, so that the corticotherapy can be supplemented, if necessary, by antiulcerous or antituberculous therapy. Similarly, the blood coagulation should be watched and anticoagulants given at the first sign of hypercoagulability. Finally, the arterial pressure and the urinary sugar level should be regularly checked. These precautions should prevent the occurrence of complications. Those few that may occur in spite of them are not to be compared with the benefits to be derived from the early use of deltahydrocortisone, which is the only method now available by which the development of icterogenic hepatitis can be halted at the start.

Iproniazid Hepatitis: Report of Five Cases and Review of Pertinent Literature. A. Felix, E. Schwartz and H. Rifkin. A. M. A. Arch. Int. Med. 104:72-82 (July) 1959 [Chicago].

The authors review the literature concerning liver damage in patients treated with iproniazid, and present a report on the occurrence of hepatocellular jaundice in the course of iproniazid treatment in 4 patients. A 5th patient is also reported, who had no jaundice but in whom widespread focal necrosis of the liver was found at autopsy, which was attributable to iproniazid therapy. Jaundice has occurred in patients receiving a wide range of dose levels. Whether the total cumulative dose given or the daily dosage is significant in determining the onset of jaundice is not clear. Evidence of liver-cell injury and jaundice usually occurs only after 2 weeks of iproniazid treatment, and generally is delayed for several weeks. The degree of liver damage may vary from mild, transient alterations of liver function tests to overt jaundice and potentially fatal, widespread hepatic necrosis and hepatic coma. There is no specific treatment other than the recognized regimens for severe hepatic damage, including steroid therapy.

The pathogenesis of liver damage due to iproniazid is still unknown. Similarly, the relation of hepatitis due to iproniazid to that caused by a virus is not clearly understood. The possibility of a direct chemical hepatotoxicity, however, cannot be disregarded. The action of iproniazid as a potent inhibitor of amine oxidase, its chemical relation to hydrazine, and its possible involvement in the metabolism of pyridoxine suggest several ways in which it may exert a toxic effect on the liver. The effects of increased circulating amines, the possibility of heretofore unrecognized inhibition of other enzyme systems, and the possibility of interference in the metabolism of vitamin B complex, all require consideration as possible pathogenic factors in the production of liver damage by iproniazid. In view of recent clinical experience, iproniazid should undoubtedly be considered a potential hepatotoxic agent. Appropriate precautions in its clinical use should be taken. It is best to withhold the drug from patients with liver disease until the effects of iproniazid therapy in such patients have been adequately studied.

Oral Treatment of Diabetes Mellitus with 1-Cyclohexyl-2-*p*-Tolylsulfanylurea: The Behavior of Serum Cholesterol During the Course of Treatment. B. D'Alessandro, A. Brancaccio, R. De Luca and G. Jacono. Minerva med. 50:1422-1426 (May 12) 1959 (In Italian) [Turin, Italy].

The authors studied the effect of Diaborale (1-cyclohexyl-2-*p*-tolylsulfanylurea), a new Italian preparation with hypoglycemic effect administered orally, on the serum cholesterol of 16 diabetic patients divided into 2 groups. The first group was composed of 11 patients with mild or moderate diabetes, who had not been treated with insulin before they were given oral treatment with Diaborale. The second group was composed of 5 patients who had been treated with insulin for a prolonged period. The values of cholesterolemia, though high in both groups, did not reach levels higher than normal. An almost total normalization of the values of glycemia was obtained during treatment with Diaborale in the patients of the first group. In these patients a slight decline in total cholesterol level, noticed early in the course of the treatment, was followed later by an increase which at times reached values higher than those noticed at the beginning of the treatment. No changes in total cholesterol level were observed during the treatment in a patient who had presented subnormal total cholesterol values in the beginning. The values of total cholesterol became normal in another patient who also presented subnormal values in the beginning. Ester cholesterol followed the same pattern as that of total cholesterol in 3 patients; the increase in the values of ester cholesterol in these patients occurred at the expense of the free cholesterol which decreased. The increase in the values of total cholesterol coincided with an increase of the values of free cholesterol in 6 patients.

The values of cholesterol increased after withdrawal of insulin in 2 patients of the second group; during treatment with Diaborale, however, these values declined and were lower at times than the values observed at the beginning of the treatment. In one of these 2 patients glycemia responded to treatment with Diaborale and became normal; the values of ester cholesterol decreased, and those of free cholesterol increased slightly. Diaborale had no effect on the values of glycemia in the other patient; the level of total cholesterol remained unchanged; the level of ester cholesterol increased; and the level of free cholesterol declined.

A decline in the values of total cholesterol was observed in 3 patients of the second group who had discontinued taking insulin for some time or were taking it only at intervals; during the course of the treatment with Diaborale these values increased to a level higher than that present at the beginning in one of these patients. A decline in total cholesterol level was observed in the other 2 patients in whom Diaborale had no effect on the values of glycemia. Free and ester cholesterol values followed the same pattern as total cholesterol, except in one patient in whom an increase in the value of free cholesterol was observed. The authors believe that prolonged treatment with hypoglycemic drugs may result in a slow accumulation of the drug in the tissues and may cause some functional alterations, which are probably reversible, in the alpha cells of the pancreas.

PATHOLOGY

Laboratory Investigations on Occurrence of Pathogenic Staphylococci in Hospital Milieu. T. M. Vogelsang. Tidsskr. norske lægefor. 79:517-523 (May 1) 1959 (In Norwegian) [Oslo].

Hospital infections due to pathogenic staphylococci have also increased in Norway. With the large number of antibiotic-resistant staphylococci which continue to occur in hospitals such epidemics can be expected to increase in frequency. When staphylococcus infections appear in a hospital department, cooperation between the division and the bacteriological laboratory should be established as quickly as possible. Specimens from all infectious foci and from nose and throat of personnel and patients should be submitted for laboratory examination. Supplementary examinations may be necessary. The isolated staphylococcus strains are typed. If the examination is made early in the epidemic, perhaps only one or two persons are carriers of the epidemic strain. If patients are carriers they must be properly isolated. If members of the personnel are carriers they should be granted leave for a time. Since many persons are intermittent carriers, there is thus a good chance that the epidemic strain can disappear from the upper respiratory tract during the stay away from the hospital.

How Reliable Is Biopsy of Rectal Polyps? A Clinical and Morphological Study of 107 Cases. C. A. Hellwig, and E. Barbosa. Cancer 12:620-624 (May-June) 1959 [Philadelphia].

The authors aimed to determine how reliable biopsy of rectal polyps is in helping the surgeon decide between abdominoperineal resection and polypectomy, without minimizing the chances of a cancer cure. The gross and microscopic findings for all rectal polyps that had been examined in the laboratory of the pathology department, Hertzler Clinic and Hertzler Research Foundation, Halstead, Kan., from 1951 to 1957, were reviewed and coordinated with the clinical findings, including follow-up observation. One hundred forty-two polyps were removed from 107 patients. Eighty-seven adenomatous polyps were regarded as benign, 28 as malignant, and 12 as invasive carcinomas. In addition, 15 biopsy specimens were diagnosed as villous papillomas, 5 of them as cancerous. Most investigators agree on the importance of removing the whole polyp for careful histological examination. Particularly in pedunculated tumors, the necessity of having the whole pedicle available for microscopic study seems generally recognized.

The biopsy material available to the authors was far from ideal with regard to the completeness of the lesions. They more often received small bits of tissue than a polyp in its entirety. Seldom did they see a polyp with pedicle intact. Follow-up observations were successful in 90 of the 107 cases (84%). A second specimen was obtained from 37 patients, either as a second biopsy or by radical resection. The remaining patients had the polyps removed by electric snare and fulguration of the base. There was complete agreement between biopsy and final diagnosis in 79 of the 90 cases, partial agreement in 7 cases, and disagreement in 4 cases. The 90 patients on whom there was complete follow-up included 20 with noninvasive carcinoma who had polypectomy and in whom invasive carcinoma did not develop. The results of biopsies in villous papillomas were disappointing. In 3 instances, the biopsy specimen showed atypia or carcinoma in situ, while the examination of the resected specimen revealed carcinoma that had spread to the submucosa. A specimen from one adenomatous polyp was diagnosed as atypia, while a second biopsy and the final specimen showed a highly malignant invasive adenocarcinoma.

The authors emphasize that atypia, cancer in situ, and intramucosal focal carcinoma in rectal polyps should not be diognosed as adenocarcinoma. Except in cases in which a high grade of malignancy is present, a diagnosis of cancer is not justified when no invasion of the submucosa can be demonstrated. Biopsy diagnosis of villous papillomas is often unreliable, because focal areas of cancer may be present in the center of the lesion, while the peripheral portions are benign. In 4 of our 12 invasive carcinomas, the first biopsy revealed benign or atypical changes, while the second biopsy or the resected specimen showed invasive carcinoma. Small size, or the presence of a pedicle, is no guarantee that a given polyp is benign. Regardless of a clinically benign appearance, every polyp should have an adequate biopsy before it is destroyed by fulguration.

Lesions in Upper Portion of the Gastrointestinal Tract Associated With Intracranial Neoplasms. J. A. Spencer, C. G. Morlock and G. P. Sayre. Gastroenterology 37:20-27 (July) 1959 [Baltimore].

At autopsies performed at the Mayo Clinic between 1946 and 1951, acute lesions of the upper part of the alimentary tract, such as petechiae. ecchymoses, ulcerative esophagitis, erosions, acute ulcers, and autolysis, were found in 148 (54%) of 274 unselected consecutive patients with intracranial neoplasms. These acute lesions of the upper part of the alimentary tract were found in only 173 (26%) of 666 patients with no significant intracranial lesions who served as controls. The incidence of coexistence of intracranial neoplasms and acute lesions in this part of the digestive tract thus has been much higher than could be expected to occur statistically by chance alone. The intracranial neoplasms in the 274 patients were interpreted as representative intracranial lesions, since in 255 (93%) complicating intracranial factors, such as infarcts, edema, hemorrhage, infection, demyelinizing disease, or surgical defects, were present. Extracranial factors which could have induced the lesions of the digestive tract were present in 82 (55%) of the 148 patients who had coexisting gastrointestinal lesions and intracranial neoplasms. These complications lend some doubt to the significance of the high incidence of coexistence of these lesions as observed in this study.

Type and location of the intracranial neoplasms could not be correlated with the acute lesions of the gastrointestinal tract. Acute changes of the upper part of the alimentary tract were found in only 50% of the patients in whom a gross pathological process involved the hypothalamus, and only 23% of the patients with acute lesions of the upper portion of the digestive tract had gross involvement of the diencephalon. Acute intracranial lesions other than increased intracranial pressure and cerebral edema were more frequently associated with acute gastrointestinal changes than were subacute or chronic intracranial lesions or the absence of lesions. Attempts to correlate clinical and pathological findings were unsuccessful. Except when gastrointestinal bleeding became evident, the presence of acute gastrointestinal complications of intracranial neoplasms could not be predicted clinically. Acute lesions of the digestive tract probably were a decisive factor in the death of 16 patients with intracranial neoplasms. Chronic and healed peptic ulcers were not found any more frequently in patients with intracranial disease than in those without intracranial disease and, therefore, should not be classified as "Cushing ulcers."

Intracranial Infections Causing Esophagomalacia and Gastromalacia: A Postmortem Study of Eleven Cases (V. Ulcer and Brain). J. B. Dalgaard. Gastroenterology 37:28-34 (July) 1959 [Baltimore].

The author reports on 6 female and 5 male patients, between the ages of 2 months and 77 years, with cerebromeningeal infections who died and in whom acute peptic ulcers were found at autopsy performed at the University institutes of pathology in Aarhus, Denmark, and Bergen, Norway, between 1949 and 1956. These 11 cases were observed among 3,000 autopsies, including 60 cases of cerebromeningeal infections. Of the 11 patients, 2 had tuberculous meningitis, 3 had nonspecific meningitis, 2 had complicated cerebral abscesses, and 4 had encephalitis which was associated with toxoplasmosis in 1. Three patients were infants less than 1 year old, and 2 others were children, 7 and 8 years old. Of the 11 patients, 10 had the type of peptic lesion known as perforating esophagomalacia or gastromalacia. Infectious cerebral lesions seem especially prone to induce this type of peptic lesion. Such lesions are agonal but are always initiated during life; the actual perforation may occur before death (often being the ultimate cause of death) or it may occur after death. Intracranial infection is an uncommon but typical cause of neurogenic peptic ulceration.

The Preservation of Human Bone Marrow at —79 C. U. Torelli. Minerva med. 50:1390-1392 (May 9) 1959 (In Italian) [Turin, Italy].

Human bone marrow remains viable for 4 or 5 days when stored at 4 C temperature and for about 2 weeks when kept in a culture. Viability can be maintained for a much longer period of time by suspending the bone marrow in a glycerol solution and freezing it at a —79 C temperature. The author describes an apparatus which he has prepared for storing human bone marrow at a low temperature. The apparatus, basically similar to that used by

Polge and Lovelock, consists of a Dewar flask of 4,500-ml. capacity. The cover of the flask is made of zinc and has a cylindrical container of 90-mm. diameter, also made of zinc, on its inner side. A smaller cylindrical container, made of copper, with a 300-ml. capacity, is placed inside the zinc container. A 100-watt resistor, through which passes a current whose intensity is regulated by a rheostat, occupies the space between the 2 cylindrical containers.

The Dewar flask is filled with a mixture of alcohol and dry ice; the space between the 2 cylindrical containers is filled with glycerol, and the internal container is filled with alcohol. The bone marrow mixed with an equal quantity of glycerol is put in vials, and these are submerged in the alcohol of the inner container. The current is turned on, and the cover is placed on the flask, so that the large zinc container is immersed in the alcohol. the temperature of which has been reduced by the dry ice to —79 C. The resistor prevents a sudden drop of temperature inside the smaller container. Freezing inside this container occurs at the rate of 1 C every 90 seconds from 0 C to —20 C and at the rate of 5 C per minute from —20 C to —60 C, after which the temperature falls rapidly to —79 C.

Normal temperature is restored to the contents of the vials by immersing them in a 37 C bath. The bone marrow separated from the glycerol is put into an empty Baxter flask, and 10 ml. of a 33% glucose solution is added for every 20 ml. of bone marrow; the contents are agitated for a few minutes, and later 30 ml. of Tyrode's solution is added for every 20 ml. of bone marrow. After a 2-minute rest an additional 120 ml. of Tyrode's solution is added, and the suspension is ready to be injected into the cubital vein. The author believes that this method of prolonged preservation will make human bone marrow available not only for homologous grafts but also for autogenous grafts.

Bilateral Cortical Necrosis of the Kidneys in the Course of Malignant Arterial Hypertension. J. C. Pimentel and R. do Rosário. Gaz. méd. port. 12: 384-394 (Jan.-Feb.) 1959 (In Portuguese) [Lisbon].

Bilateral cortical necrosis of the kidneys is frequently found in women in association with pregnancy, but it may also occur in men and be associated with chemical intoxications or infectious diseases. The authors report on a case in which bilateral renal necrosis occurred in association with malignant arterial hypertension; they believe that this is the second case of this nature to appear in the medical literature. A 54-year-old man was admitted to the Gama Pinto Institute in Lisbon because of gradual loss of vision and mental confusion. He presented a history of arterial hypertension of a few years' duration and had lately been suffering from persistent headache, anorexia, dizziness, ear buzzing, and insomnia.

The diagnosis of malignant arterial hypertension was made, and the patient was treated with sedatives, intramuscularly administered papaverine, intravenously administered hypertonic dextrose solution, and parenteral feeding. His condition deteriorated in spite of the treatment. Anuria and coma occurred, and the patient died 5 days after admission to the hospital. At autospy the pathological findings revealed necrosis in all the structures of the renal cortex (glomeruli, tubes, vessels, and interstitial tissue) in association with the lesions that are typical of malignant arterial hypertension. The authors believe that the vascular lesions characteristic of malignant arterial hypertension may cause unilateral or bilateral renal necrosis, depending on whether or not the hypertensive condition has a renal origin.

Hormones and Carcinogenesis. O. Mühlbock. Nederl. tijdschr. geneesk. 103:949-952 (May 2) 1959 (In Dutch) [Amsterdam].

The question whether hormones can exert a carcinogenic effect has been repeatedly investigated in recent years, and some published reports of such studies are cited by the author. A survey revealed that hormones presumed to be carcinogenic all have growth stimulating effects. Thyroid tumors have been produced experimentally by thyrotropic hormones; tumors of the adrenals, by the adrenocorticotropic hormone (ACTH); and various types of ovarian and testicular hormones, by gonadotropic hormones. It should be remembered, however, that the commercially produced hormones are derived from slaughtered animals, and, as a result, type specificity and antibody formation are involved in their action. In the female secondary sex organs, such as the breast and uterus, tumors have been produced by estrogenic hormones. Breast tumors have also been produced by the mammotropic hormone of the hypophysis. Hormones of the hypophysis with stimulating effects on organs such as the gonads, adrenals, or thyroid take first place among hormones with carcinogenic effects, and the steroid hormones are second in importance. Hormones such as insulin and thyroxin, which influence the metabolism in general but not a specific organ, have no carcinogenic effect. The somatotropic or growth hormone also has a systemic metabolic effect, but it has been possible to induce tumors in rats with pure growth hormone; the tumors thus produced ranged from sarcomas and adenocarcinomas to lymphoid tumors.

Whereas the connection between growth stimulation and carcinogenic effect is clear in endocrine organs and in secondary sex organs, it is doubtful in other organs and in lymphoid tissue. The action of estrogenic hormones as leukemia-inducing factors is still obscure, and likewise obscure is the mechanism by which skeletal and liver tumors develop under the influence of hormones. There is some evidence that the action of estrogenic hormones on the renal tubules of hamsters can be interpreted as a growth stimulus, which may be the first step in the development of renal tumors.

The carcinogenic effect of a hormone is largely dependent on the amount of hormone that acts on an organ. For instance, estrogenic hormone may induce breast cancers in castrated male mice; if the amount given is only equal to that physiologically present in female mice, relatively few breast tumors develop and at a rather advanced age; if, however, a dose 16 times as great is administered, breast tumors develop in all animals and at a younger age. The author's own studies, reported some years ago, revealed that the sensitivity of the organ to hormone effects also is important, in that with high sensitivity normal amounts of hormone may cause tumor formation. Furthermore, the author and a co-worker also observed a difference in the carcinogenic effect of a hormone, depending on whether the hormone was given continuously or interruptedly, the incidence of tumor development being much greater with continuous administration. Finally, the time of life during which hormones are given is important; thus, whereas hormone administration begun early in life produces breast tumor in a high percentage of patients, when the hormones are given during the second half of life, they exert a carcinogenic effect only occasionally. Hormone administration is usually given to middle-aged persons.

The Early Lesions of Aortic Atherosclerosis in Cali, Colombia. C. Restrepo and H. C. McGill Jr. A. M. A. Arch. Path. 67:618-623 (June) 1959 [Chicago].

This study represents one part of a continuing cooperative project between several pathology laboratories, which aims to write the natural history of atherosclerotic arterial lesions for different population groups in different geographic regions. Data of this same type derived from autopsy populations of New Orleans, Guatemala, and Costa Rica have been reported previously. The extension of this study to Colombia has been of particular interest in view of the fact that Colombia, according to vital statistics, has one of the lowest death rates from arteriosclerotic heart disease in the world.

The aortas of 289 persons, between 1 and 40 years of age, from a large charity hospital and a medicolegal service in Cali, Colombia, were quantitatively evaluated for the extent of the various types of atherosclerotic lesions. These figures were then compared with similar data for New Orleans Negroes, New Orleans whites, and Guatemalans. Fatty streaks were found to increase rapidly in extent during the second decade in Colombians, just as in other groups, and the hypothesis that this development of fatty streaks is related to the hormonal changes of puberty is supported. Despite having more fatty streaks in the third decade, the Colombians developed fewer fibrous plaques than the New Orleans whites, suggesting again that different factors control the progression of the different types of lesions. In view of the presumed relationship between lesions and clinical disease, these data on aortic lesions are not consistent with a low rate of arteriosclerotic heart disease such as is indicated by the vital statistics for Colombia.

RADIOLOGY

Radiologic Picture of the Lung in Marked Mitral Stenosis: Clinical, Hemodynamic, and Surgical Correlations. F. Galland, S. Aranda, S. Aceves and N. Dorbecker. Arch. Inst. cardiol. México 29:145-174 (March-April) 1959 (In Spanish) [México, D. F.]

The need for an accurate diagnosis of the degree of mitral stenosis, for the detection of association with other valvulopathies, and for an appraisal of the results of surgical correction has led to the present general interest in the radiologic study of the patient suffering from mitral stenosis. The authors studied 20 patients in whom mitral stenosis was either the only or the predominant pathological condition, and in whom the stenosed mitral area was smaller than 1 sq. cm. as determined by the surgeon at commissurotomy. Ten of these patients were men, and 10 were women, their ages ranging from 13 to 45 years. Besides the clinical and hemodynamic study of each patient, preoperative and postoperative teleradiograms were taken in each case, under the usual incidences (postero-anterior, right antero-oblique, and left antero-oblique). The postoperative radiograms were taken during the first 2 months after surgical intervention, then 2 to 6 months, 6 months to one year, and after one year following the operation. Clinically, the patients were classified into 4 groups according to the degree of pulmonary capillary hypertension, of dyspnea, and of size of the mitral area involved.

The preoperative picture of the lung showed hilar nebulosity in all the patients, laminar effusion in 14, horizontal scissure with abnormal characteristics in 9, lightly spotted areas in 15 and heavily spotted areas in 4 (the latter resembling the radiologic aspects present in hemosiderosis), and septal lymphatic lines (lines B of Kerley) in 17. A comparison of the clinical and radiologic pictures showed that the preoperative picture of the lung was correlated with the capillary pressure in 9 (64.2%) of the 14 patients in whom catheterization had been performed; with the clinical symptoms of venous capillary hypertension in 16 (80%) out of 20 patients; and with the size of the mitral area in 18 (94.7%) out of 19 patients. During the postoperative stage, as the patient improved and the degree of dyspnea decreased, the radiologic picture of the lung approached the normal image, showing a correlation between the clinical and the radiologic pictures in 16 (88.8%) out of 18 patients in relation to venous capillary hypertension and in 17 (94.4%) out of 18 patients in relation to the degree of mitral opening obtained. The authors conclude that, as a rule, there exists in patients with mitral stenosis a correlation between the radiologic picture of the lung, on the one hand, and the venous capillary hypertension and the involvement of the mitral area, on the other, and that the changes in the postoperative radiologic picture may serve, on the whole, as means of evaluating the effectiveness of the operation.

The Roentgenologic Evaluation of Systemic Lupus Erythematosus. T. L. Taylor and H. Ostrum. Am. J. Roentgenol. 82:95-107 (July) 1959 [Springfield, Ill.].

The authors report on findings in the roentgenograms obtained at the Philadelphia General Hospital from 23 patients with proved systemic lupus erythematosus. These findings depended on the stage of the disease during which the roentgenograms were taken, and they reflected acute or chronic inflammatory changes in the pleura, lungs, and pericardium. In the initial acute stage, these changes consisted of bilateral moderate or massive pleural effusion, massive pericardial effusion, subpleural inflammation, perivascular inflammation, small areas of interstitial pneumonitis at the lung bases, and small areas of segmental pneumonitis at the lung bases. In the resolving stage, the findings included those of minimal unilateral or bilateral pleural effusion, minimal to moderate pericardial effusion with straightening of the left border of the cardiac shadow but without widening of the heart base, small linear areas of "plate-like" atelectasis at the lung bases, and areas of segmental atelectasis at the lung bases. In the chronic stage, the chest roentgenograms showed that, unless the nephrotic syndrome was present, the cardiac outline returned to normal or cor pulmonale developed. In some patients the outline of the pulmonary conus remained particularly obscured by fibrosis which filled in the pericardial spaces around the conus. The pleural effusion may completely disappear. Fine pulmonary scars may be seen at the lung bases, frequently associated with "tenting" of the pleura, or the lungs may appear clear. Multiple pulmonary infections occurred. During period of exacerbation, pleural and pericardial effusions were limited by adhesions; fine linear densities were intermingled with small areas of interstitial pneumonia at the lung bases; basal areas of segmental pneumonitis occurred; subpleural and perivascular inflammation was present.

A history of joint pain and the pericardial, perivascular, interstitial, and pleural inflammatory changes which are visible in chest roentgenograms provide evidence which is almost pathognomonic of acute systemic lupus erythematosus. Delayed renal function may be evident on intravenous pyelography. The relationship between systemic lupus erythematosus and destructive joint changes typical of rheumatoid arthritis is unproved. In the patients of this series, there were no instances of demonstrable joint changes other than soft tissue edema and those changes attributable to Raynaud's syndrome.

Pulmonary Alveolar Proteinosis: Report of Two Cases. G. F. Lull Jr., J. C. Beyer, J. G. Maier and D. F. Morss. Am. J. Roentgenol. 82:76-83 (July) 1959 [Springfield, Ill.].

The authors report on a 23-year-old man and on a 40-year-old woman with pulmonary alveolar proteinosis, a disease which was first described by Rosen in 1958, and 28 cases of which were collected from the literature. The name of the disease is a misnomer in that the intra-alveolar substance is not a protein, but until the substance is accurately identified, the name will remain. The causation of the condition is unknown. Whether it is a truly new disease has not been established, but it appears not to have been present before 1953, and it has been recognized with increasing frequency since then. The changes revealed by the chest roentgenograms of the 2 patients were strikingly similar to those reported by other workers. The characteristic appearance has been that of a fine granular or feathery type of parenchymal density, soft in appearance and usually widely disseminated. Its radial distribution from the lung hili resembled severe pulmonary edema in the collected cases, while in the authors' patients this radial distribution was not especially apparent, and the densities tended to be increased in number and to be more confluent toward the lung bases.

Both patients were subjected to thoracotomy for lung biopsy. A single wedge of tissue was removed from the right middle lobe of the man and wedges were removed from the apical posterior segment of the upper lobe and from the lingula in the woman. In both patients, there were patchy, confluent areas of a granulomatous-like process without evidence of discrete nodules or of caseation, and with interspersed areas of grossly normal lung parenchyma. Microscopically, there was a patchy, alveolar filling process with the material consisting of a granular acidophilic substance which was PAS-positive. The interalveolar septums were not involved per se, but proliferation of large cells, somewhat like lipophages, was noted from the alveolar walls. These were interpreted as septal cells, and granules within their cytoplasm were also PAS-positive. While histopathological diagnosis is required to confirm the diagnosis, pulmonary alveolar proteinosis may be suspected in a patient who shows extensive pulmonary changes on the chest roentgenogram in the presence of essentially normal findings on physical examination of the chest. Inasmuch as pulmonary alveolar proteinosis is being seen with increasing frequency, since it is a chronic disease, and inasmuch as there appears to be a high mortality rate, with deaths resulting from superimposed infection or from obliteration of the respiratory surface, the search for the causative agent and for adequate therapeutic measures must be pressed with vigor.

Idiopathic Unilateral Hyperlucent Lung: A Roentgenologic Syndrome. H. N. Margolin, L. S. Rosenberg, B. Felson and G. Baum. Am. J. Roentgenol. 82:63-75 (July) 1959 [Springfield, Ill.].

The authors report on 4 male patients, aged 12, 25, 28, and 40 years, respectively, with abnormal radiolucency of an entire lung or lobe which could not be classified among the usual entities known to cause this appearance. In addition to the abnormal translucency mentioned, the chief roentgen-ray features included normal or small size of the affected lung or lobe; maintenance of almost constant volume of the affected portion of the lung during changes in respiration; a small hilar shadow with sparseness of the intrapulmonary vascular markings; and an unusual bronchiectatic pattern without evidence of obstruction of the larger bronchi. This combination of the roentgen-ray signs of unilateral emphysema, a normal main bronchus (supplying the affected portion of the lung) but abnormal small bronchi, and a diminished intrapulmonary vascular pattern resulted in a readily recognizable complex, which appears to represent a genuine roentgenologic entity, for which the term "idiopathic unilateral hyperlucent lung" is suggested. Not enough is known of its pathogenesis to justify a more specific title.

The clinical and laboratory aspects of the condition indicated that it is associated with a disability of varying degree, perhaps related to impairment of pulmonary function. Differentiation of this syndrome from other conditions causing abnormal unilateral radiolucency can be made, bronchography being of particular value in this regard. The question of separating unilateral hyperlucent lung from the entity of hypoplasia of a pulmonary artery deserves particular consideration, since the diagnosis of hypoplasia of a pulmonary artery is very difficult. Although all 4 patients appeared to show unilateral deficiency in pulmonary arterial circulation, it is believed that hypoplasia of a pulmonary artery is probably a separate entity from idiopathic unilateral hyperlucent lung, but an absolute differentiation between them may not be possible until there is further knowledge of the pathogenesis and causation of these conditions.

Blood Counts in Relation to African X-Ray Staff. E. F. Allen, A. Cruickshank and L. R. Whittaker. East African M. J. 36:274-275 (May) 1959 [Nairobi, Kenya].

Total and differential white blood cell counts were routinely made on staff exposed to ionizing radiations in the x-ray department of the King George VI Hospital, Nairobi, Kenya. It was found that, in comparison with accepted European constants, the blood counts of the European staff were within normal limits, while in the African staff relative leukopenia and lymphocytosis were common. Leukopenia and a relative lymphocytosis can suggest an early blood change due to ionizing radiations; however, by direct monitoring it was found that none of these members of the staff received exposure greater than 0.025 rad per week. Therefore, as a baseline for future analysis of the leukocyte counts of the African staff of the x-ray department, the total and differential leukocyte counts of 80 students from the Medical Training Center in Nairobi were determined. The results obtained demonstrated that, in assessing a possible radiation hazard, the standard accepted as normal for the European staff cannot be applied to the African staff. The standard quoted in this paper is applicable to Nairobi (altitude, 5,000 ft.) and will not necessarily apply in other areas. Radiation monitoring by the film method is the most accurate method available and should be regularly observed on staff exposed to ionizing radiations. Nevertheless, quarterly routine total and differential blood counts should be taken in order to ascertain that there is no individual susceptibility to ionizing radiation.

PUBLIC HEALTH

The Case Against B. C. G. A. S. Anderson, L. B. Dickey, M. L. Durfee and others. Brit. M. J. 1:1423-1430 (June 6) 1959 [London].

Tuberculosis differs from smallpox in that an attack does not result in dependable immunity. Thus there is slim premise for attempting to produce immunity artificially. Allergy to tuberculoprotein is not an indication of immunity, but is a prerequisite to the development of clinical tuberculosis. The human body defends itself better against first invasions with tubercle bacilli than it does against reinfections. Clinical disease develops only in persons who have been previously sensitized to tuberculoprotein. Accurate differentiation between primary pulmonary infiltrates and clinical lesions of reinfection type is of the utmost importance. Without this, erroneous deductions are made with reference to efficacy of BCG vaccine. For example, it may be credited with beneficial effects when primary infiltrates are grouped with lesions of reinfection type, so it appears that clinical disease develops in more control persons than in those in whom primary lesions have been produced in the skin by BCG vaccine. An adequately controlled study of BCG vaccination among people living in their homes has never been accomplished. It has been found impossible. However, well-controlled studies were conducted among the cattle herds in the United States and Canada and elsewhere. BCG vaccine failed and was abandoned. In the few places in which it is still used with major dependence on it, tuberculosis remains a serious problem among cattle.

Among human beings the most phenomenal accomplishments in eradication of tuberculosis have been achieved in countries in which little or no BCG vaccine has been used, including Iceland, Hawaii, and the Netherlands. In countries in which BCG vaccine has been employed extensively, including Denmark, Norway, and Sweden, marvelous results have been achieved, but along with BCG vaccine there have been employed the same fundamental methods which alone brought about the greatest accomplishments in history. This also applies to special groups such as students of nursing and medicine. The numerous values of the tuberculin test in diagnosis and epidemiology are lost to persons whose tissues have been sensitized to tuberculoprotein by BCG vaccine. Bacteriological investigations have revealed that cultures designated BCG. were not composed of just a single bacterial form such as Calmette and Guérin produced, but of multiple bacterial forms, which differed in many of their properties, and some of which were definitely invasive for animal tissues. No two cultures were alike. Evidently different mutants and changes had occurred in each of the cultures studied. Apparently mutants produced destructive disease in animals on deficient diet, those which were silicotic, and in at least two species of normal animals. In human beings, they sometimes caused lesions at the site of administration and of regional lymph nodes, as well as other organs, and death in at least a few cases. Calmette repeatedly warned that no living organism capable of producing tubercles in animal tissues should be administered to human beings. If methods of preventing mutations in cultures have been or can be devised, there is no assurance that it will not occur after the living organisms are introduced into human tissues.

The 17 American workers who wrote this review believe that inasmuch as most BCG proponents recommend it only for those uninfected, it would not be applicable to the about 56 million citizens in the United States who already are tuberculin reactors. Moreover, among the remainder the tuberculous infection attack rate has reached such a low ebb that relatively few would be expected to become infected. Furthermore, treatment now available is effective for recently developed clinical lesions.

Long-term Effectiveness of B. C. G. Vaccination of Infants in Close Contact with Infectious Tuberculosis. J. Lorber and P. C. Menneer. Brit. M. J. 1:1430-1433 (June 6) 1959 [London].

The authors report on 267 children who were aged less than 2 years when they were vaccinated with BCG vaccine between 1949 and 1952. Of the 267 children, 261 were followed up 5 or more years after their vaccination. Of these, 10 (3.7%) were alive and well, but their parents refused reexamination. Three (1.1%) had died of other causes than tuberculosis. The remaining 248 (92.9%) were reexamined and tuberculin-tested, and chest roentgenograms were obtained from 235. There were no deaths from tuberculosis. Only 2 had minor clinical symptoms associated with tuberculous lung lesions which healed by calcification, and one additional child had a calcified lung lesion. Only 4 of the 248 children on whom tuberculin tests were performed had reverted and were tuberculin negative. The 4 negative reactors were revaccinated and they responded with a typical primary BCG lesion like tuberculin-negative children.

All of the vaccinated children were household contacts of tuberculous persons including parents, grandparents, and other persons. In contrast to the children, 39 (15.7%) of these tuberculous persons died of their tuberculosis and 28 (11.3%) still had active disease at the time of the follow-up. As there were no comparable controls it cannot be shown conclusively that BCG vaccination prevented tuberculosis in this group of children. Nevertheless, the results obtained are highly suggestive that this was the case. The facts that from such a particularly unfavorably situated group of infants none died of tuberculosis and that symptoms which could possibly be attributed to tuberculous infection developed in only 2 suggest that the vaccinations were of value. The prolonged effectiveness of the vaccination, as judged by the persistence of the positive tuberculin reaction in 98% of the children retested, is emphasized.

BOOK REVIEWS

Nutrition and Atherosclerosis. By Louis N. Katz, M.D., Director, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago, Jeremiah Stamler, M.D., Director, Heart Disease Control Program, Chicago Board of Health, and Ruth Pick, M.D., Assistant Director, Cardiovascular Department, Medical Research Institute, Michael Reese Hospital. Cloth. $5. Pp. 146, with 67 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1958.

This is the second monograph concerned with atherosclerosis from the Medical Research Institute of Michael Reese Hospital. Like the first, its value rests especially in the list of references—a nearly complete register of the scientific literature dealing with atherogenesis to the middle of 1958; the earlier monograph had carried them as far as 1953. Beyond this catalogue of references the monograph has some serious limitations. The authors tend to be preoccupied with their own publications. This is understandable, but when, as often happens, the authors cite one of their own reviews as a source which is as readily available in its original form I think they do an unscholarly thing. Most scientists will not need these authors for interpreters.

The authors begin with a statement of a theory that is, frankly, a corker. It is, in the first place, a monumental problem for grammarians—"the nutritional-metabolic cholesterol-lipid-lipoprotein theory of atherogenesis." This seems to take care of almost any eventuality. To say that atherogenesis is influenced by nutritional and metabolic factors is surely conservative, one might even say trite. The authors say, in describing this theory, "The atherogenic alterations . . . are by-products of an habitually unbalanced diet excessive in total calories, empty calories, total fats, saturated fats, cholesterol, refined carbohydrates, salt and inadequate (relatively and/or absolutely) in certain essential nutrients (vitamins, minerals, essential amino acids and essential fatty acids) and in bulk." The fact that these authors can find nothing good about the finest diet in human history is perhaps the tip-off to their limitations in preparing such a book. They are not familiar with the science of nutrition and they seem to view this field and its problems in a superficial way. One of them is a physiologist and cardiologist; another is somewhat harder to classify but in this report he writes like an epidemiologist. Both are experienced poultry men. These circumstances lead to several unsound statements and interpretations.

The Life and Times of Sir Charles Hastings, Founder of the British Medical Association. By William H. McMenemey, M.A., D.M., F.R.C.P. Boards. $10. Pp. 516, with illustrations. [Williams & Wilkins Company, 428 E. Preston St., Baltimore 2]; E. & S. Livingstone, Ltd., 16 and 17 Teviot Pl., Edinburgh 1, Scotland, 1959.

This is the biography of the man who in 1832 founded the Provincial Medical and Surgical Association in Worcester, the oldest association of general practitioners in England. Since this later merged with other local medical societies to form the British Medical Association, Hastings is credited with being its founder. In those days as in modern times there were many heated controversies involving medical standards, general policy, and laws related to medical practice. Hastings took an active part in all such matters and for many years served as a secretary of the Provincial association. The style of this biography is leisurely, and it should appeal to those who have a special interest in medical history. Furthermore, in anyone who has lived in the Midlands it is sure to awaken pleasant memories. At the end of the volume there is a bibliography of Hastings' writings, a general bibliography, and an index.

Medical Department, United States Army. Cold Injury, Ground Type. By Colonel Tom F. Whayne, Professor of Preventive Medicine, School of Medicine, University of Pennsylvania, Philadelphia, and Michael E. DeBakey, M.D., Professor of Surgery and Chairman of Department, Baylor University College of Medicine, Houston. Prepared under direction of Major General S. B. Hays, Surgeon General, United States Army. Editor in chief: Colonel John Boyd Coates, Jr. Associate editor: Elizabeth M. McFetridge, M.A. Office of Surgeon General, Department of Army, Washington, D. C. Cloth. $6.25. Pp. 570, with illustrations. Superintendent of Documents, Govern. Print. Off., Washington 25, 1958.

This book, one of the volumes which comprise the official history of the medical department of the United States Army in World War II, is essentially a history of the experience with cold injuries encountered in the various theaters of operations. There is little doubt that the statement in the foreword "that this is the most comprehensive volume on the ground type of cold injury that has ever been published" is correct. The further statement that, if the experience here recorded is given due consideration there should be no similar experience in future wars, seems equally well-founded. The book is beautifully illustrated and written in a most interesting manner. The reader will be staggered at the magnitude of disability caused by cold injury during World War II, and at the multiple problems of supply of clothing and distribution of infor-

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

mation which led to the development of this experience. No attempt is made to whitewash the many errors in judgment made by high-ranking officials which seem altogether obvious in retrospect. The armchair tactician should find the correlation of battle circumstances with the development of cold injuries most interesting.

A number of the chapters should be of particular interest to the nonmilitary physician. Those on General Consideration of Cold Injury, Pathogenesis and Pathologic Process, Clinical Picture and Diagnosis, Therapy and Disposition Overseas, and Therapy and Disposition in Zone of the Interior should be of great value to any physician treating cold injuries. A particularly noteworthy portion of the book is that which deals with cold injuries incurred at high altitudes. The state of our knowledge concerning these injuries is far from complete, and the current answer to the problem lies in prevention rather than treatment of these lesions. This volume should be required reading for the military surgeon as well as for persons in positions of command in the armed forces.

Youth and Fitness: A Program for Secondary Schools. Report of National Conference on Fitness of Secondary School Youth, December 7-12, 1958, Washington, D. C. Paper. $1.50; discounts on quantity orders. Pp. 74, American Association for Health, Physical Education, and Recreation, a department of National Education Association, 1201 16th St., N. W., Washington 6, D. C., 1959.

This report of a conference sponsored by the American Association for Health, Physical Education, and Recreation includes the keynote address by Shane MacCarthy, executive director of the President's Council on Youth Fitness, and a speech by Wayne O. Reed, deputy commissioner of the U. S. Office of Education. There are special groups of recommendations in relation to health education, physical education, boys athletics, girls physical activity program, recreation in general, and outdoor education. Other contributions were "The Social and Economic Setting for American Education" by Marion Clawson of the Ford Foundation; "Advances in Health and Medical Sciences" by Aims C. McGuinness, M.D., assistant to the secretary of the U. S. Department of Health, Education, and Welfare; "The Growth and Development of Today's Adolescent" by Prof. John J. Kurtz of the University of Maryland; and "The Role of the American Secondary School" by Paul E. Elicker, executive secretary of the National Association of Secondary School Principals.

Although the purpose of the conference included the discipline of medicine and its representation along with public health, recreation, athletics, and child growth and development, a check of the list of participants reveals only three physicians. The medical aspects of the various subjects covered are touched on only sketchily. The section on physical education, for example, contains among the essentials of a desirable physical education program sections on attitudes, knowledge, skills, administrative provisions for physical education, and general recommendations, but no reference to the importance of medical examination for athletes or participants in physical education or the importance of injury prevention or emergency service to injured or ill participants.

Office Orthopedics. By Lewis Cozen, M.D., F.A.C.S., Attending Orthopedic Surgeon, Cedars of Lebanon Hospital, Los Angeles. Third edition. Cloth. $9.50. Pp. 430, with 321 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1959.

This book covers such subjects as physical therapy, legs, arms, back, scoliosis, neck, clubfoot, limp, flat foot, bowlegs, and knock knees. The table of contents is confusing. One might question the inclusion in this book of a discussion of painful jaw. The section on scoliosis is poor and the section on the law court is grossly inadequate. The author's consideration of stellate ganglion block as a routine office procedure is highly questionable. The value of hydrocortisone is overemphasized. Prosthesis fitting is hardly an office procedure. The proof reading is poor. The quality of the illustrations ranges from superb to amateurish. The author's excellent qualifications are not reflected in his book. He fails flagrantly to credit original sources of text and illustrations; he furnishes an extensive bibliography and states that he has read every article listed. It is unbelievable that a man could have read so much good material and still give his readers so little. The book does not fill a need, niche, or vacuum.

The Barbiturate Withdrawal Syndrome: A Clinical and Electroencephalographic Study. By Munke Hertel Wulff. [Thesis, M.D., University of Copenhagen.] Issued simultaneously as Electroencephalog. & Clin. Neurophysiol., supp. no. 14. Paper. Pp. 173, with 19 illustrations. Ejnar Munksgaard, Nørregade 6, Copenhagen, K, Denmark, 1959.

This monograph, the first of its kind, presents useful information for both the clinician and the researcher. The subject matter should appeal to a wide cross section of specialists in both fields. The author deserves credit for collating data on 78 chronically addicted barbiturate users as well as 40 patients who are used for comparison and control. The study represents more than five years of research.

The historical and introductory data are well presented in text and tables without being too lengthy. Throughout the monograph liberal use is made of clearly presented figures and tables. Methods are well described, and the use of controls is notable throughout. The monograph is comprehensive in that clinical, pharmacological, chemical, neuropathological, and electroencephalographic data are included. The idea is presented that the barbiturates which disappear slowly from the blood are less likely to induce major abstinence manifestations on abrupt withdrawal. The use of photic stimulation to induce paroxysmal electroencephalographic changes during withdrawal of barbiturates is presented, and its experimental and clinical utility made apparent.

The final chapter is devoted to conclusions and practical implications. In addition, there is a nine-page summary in Danish. An appendix with selected case studies presented in text and table form is another useful feature. The list of references is comprehensive, and an index is provided. This monograph is unequivocally recommended and should be especially useful to neurologists, psychiatrists, electroencephalographers, and pharmacologists, but the multidisciplinary approach and comprehensive nature of the work give it a flavor which should prove interesting to a wide variety of readers.

Handbook on Standard Nomenclature of Diseases and Operations. By Edward T. Thompson, M.D., editor, Standard Nomenclature of Diseases and Operations, and Adaline C. Hayden, C.R.L., associate editor. Prepared for American Medical Association. Paper. $1.50. Pp. 71. Blakiston Division, McGraw-Hill Book Company, Inc., 330 W. 42nd St., New York 36; 95 Farringdon St., London, E. C. 4, England. 253 Spadina Rd., Toronto 4, Canada, 1959.

The chief aim of this handbook is to present in simple form the basic principles of terminology and a brief analysis of nomenclature. This booklet can be easily carried in the pocket and should be of special value to the intern and resident. Nothing concerned with the nomenclature of diseases and operations is more important than that an acceptable standard be compiled and used. Unfortunately, differences of opinion among experts and changing concepts of disease necessitate constant reevaluation and revision so that, although we may approach a fixed standard, we can never really achieve it. Insofar as a standard of nomenclature furthers the elimination of obsolete terms and the use of preferred terms on the widest possible scale it will have accomplished a worthy purpose.

As stated in this handbook, "in recording a diagnosis, the physician should make certain (1) that his statement is specific and complete, (2) that he names a disease entity, not a symptom of the disease, (3) that his statement does not contain eponyms or obsolete or indefinite terms, and (4) that he is not using a pathologic statement for a clinical diagnosis." A list of unacceptable eponyms and their corresponding preferred terms is included and should be most valuable. The retention of "acceptable" eponyms is deplorable and an indication that for some diseases exact diagnostic terms are still not generally agreed on. Although most of the material found in this booklet should be incorporated in "Standard Nomenclature of Diseases and Operations," it is well to have this practical handbook. It is hoped that it will be widely used.

Pathology of Tumours of the Nervous System. By Dorothy S. Russell, Sc.D., M.A., M.D., Director, Bernhard Baron Institute of Pathology, London Hospital, London, and L. J. Rubinstein, M.D., Lecturer in Morbid Anatomy, London Hospital Medical College, London. With chapter on Tissue Culture in Relation to Tumours of the Nervous System, by C. E. Lumsden, M.D., Professor of Pathology, University of Leeds, Leeds. Cloth. $13.50. Pp. 318, with 286 illustrations. Williams & Wilkins Company, 428 E. Preston St., Baltimore 2; Edward Arnold (Publishers) Ltd., 41 Maddox St., London, W. 1, England, 1959.

The author of this volume is one of the world's most outstanding neuropathologists. She has always been forthright in drawing and expressing her conclusions. Even those who have disagreed with her have admired her approach to pathological problems. This is an excellent book. It is concisely and clearly written. It is not encyclopedic, as is the much larger book by Zülch (published as vol. 3 of the "Handbuch der Neurochirurgie" in 1956), but it is adequate. It also contains appropriate bibliographic references. The photomicrographs are well chosen and clearly reproduced. The concluding chapter on tissue culture is a stimulating addition. This technique has never been fully exploited in our study of neoplasms and their treatment, and this intriguing subject is well presented here. Everyone interested in learning about tumors of the nervous system and their pathological characteristics should find this a useful book. It is recommended without reservation.

Immunopathology: 1st International Symposium. Edited by Pierre Grabar and Peter Miescher. [In English, French and German.] Cloth. $16.25. Pp. 520, with illustrations. Benno Schwabe & Co., Steinentorstrasse 13, Basel, Switzerland [Intercontinental Medical Book Corporation, 381 Fourth Ave., New York 16], 1959.

The 50 investigators, immunologists, immunopathologists, immunochemists, and clinicians who participated in this symposium in 1958 talked on inflammation, properdin, agammaglobulinemia, organ-specific immunopathology, rheumatoid arthritis, and disseminated lupus erythematosus. Some of the world's leading authorities in these new and rapidly growing fields of medical research are represented in this volume. The session was opened by Witebsky with a scholarly and sparkling sketch of the history of immunopathology, and he spoke again on his own pioneering contributions in the role of autosensitization in thyroid disease. Another American investigator, Good, spoke on agammaglobulinemia, the condition with which his name is intimately connected. Most of the other speakers were of similarly high caliber. The bulk of the book is taken up by inflammation and lupus erythematosus (160 and 150 pages respectively). For those who did not attend this symposium, reading this well-edited and documented account of what must have been an exciting and stimulating event is the next best thing.

QUESTIONS AND ANSWERS

ANAPHYLACTIC REACTION FROM TRYPSIN

To the Editor:—*An obese middle-aged woman with hypertension had been treated by another physician for a varicose ulcer of the left leg, over the tibia. Improvement over a 10-day period with use of an ointment was slow. Her ulcer became redder and more painful. I was then consulted, and I gave her an injection of 1 cc. of aqueous chymotrypsin (Chymar, 5,000 units). She had a history of a moderate reaction to penicillin. She felt very hot four or five minutes after the injection. Her blood pressure at this time was 158/92 mm. Hg. She said she felt dizzy. Simple syncope was suspected. In the next two minutes the patient felt worse and thought she would faint. She also had difficulty breathing. Her radial pulse became barely palpable and rotary nystagmus developed.*

At this time 100 mg. of hydrocortisone was injected into the site of the earlier injection. The radial pulse disappeared and the patient lost consciousness. Three or four minutes later the patient became semiconscious. Her body became covered with circular hives. Investigation at the local pharmacy showed the ointment prescribed by the first physician to be crystalline trypsin ointment (Tryptar). What is the incidence of severe sensitization to parenterally given trypsin subsequent to its topical use? How permanent is such an allergic response?

Martin L. Hauer, M.D., Lebanon, Pa.

Answer.—The ointment used contains a purified crystallized trypsin derived from mammalian pancreas. Sensitization or antigenicity to this preparation has not been reported. According to the manufacturer, it may exhibit a histamine-like effect which is easily controlled by antihistaminics. Despite this description, the sequence of events in this patient strongly points to the probability that the ointment was antigenic in nature. Since the trypsin is derived from mammalian pancreas, it certainly is a foreign protein. The sensitizing factor may be the protein of the animal whose pancreas was used in preparation of the trypsin or the pancreatic tissue protein itself.

It is likely that the repeated application of the trypsin ointment in an ulcerated area over a period of 10 days was sufficient to sensitize this patient so that subsequent injection of chymotrypsin was enough to produce anaphylactic shock. The manufacturer indicates in describing Chymar that "although sensitivity is uncommon the usual precautions should be exercised in those patients with known allergies or sensitivity."

Once present, it is difficult to define exactly the duration of such sensitivity. It may persist; hence such a person's life might be endangered by inadvertent prolonged parenteral use of chymotrypsin. Two cases reported by Criep (*J. Allergy* 12:154, 1941) indicate a shorter duration. A systemic allergic reaction occurred after the intramuscular injection of deinsulinized pancreatic tissue. Treatment was resumed after an interval of a month in one instance with but one untoward reaction, and i was subsequently continued every three or four days for a month without any symptoms. In the other case therapy was discontinued for two months after a rather mild reaction to the injection o pancreatic extract and subsequently was restarted without any trouble. Thus each case has to be evaluated individually and every precaution taken especially if the patient is constitutionally allergic.

The fact that a protein substance has its analog in the human does not mean it is not a totally foreig protein. Human beings may become sensitized t their own tissues, which may act as foreign protein when altered by infection or chemical agents.

NORMAL PROTEINURIA

To the Editor:—*What is the upper limit of norma of proteinuria in the healthy adult? Orthostati albuminuria has been ruled out, and there is n history of genitourinary disease. The sulfosalicyli acid reagent test method has been used.*

M.D., North Carolina.

Answer.—The glomerular filtrate of the kidney normally contains about 25 mg. of protein per 10 ml.; the 180 liters of glomerular fluid filtered durin the course of one day would contain 45 Gm. o protein. Addis (Glomerular Nephritis: Diagnosi and Treatment, New York, the Macmillan Company, 1949) estimated the normal protein excretio to be from 5 or 10 to 100 mg. per 24 hours. Riga and Heller (*J. Clin. Invest.* 30:853, 1951), by ultrafiltration concentration of the urine, found an average of 40 mg. of protein per 24 hours. For convenience, the daily urine volume can be assumed to be 1,000 ml., resulting in a normal concentratio of 0.5 to 10 mg. of protein per 100 ml. The sulfosalicylic acid test for proteinuria is sensitiv

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

enough to give a "faint trace" positive at 10 to 50 mg. per 100 ml. The heat and acetic acid test is more sensitive, detecting 1 to 3 mg. per 100 ml. in "clear" urine against a black background; 1 to 10 mg. per 100 ml. is the usual range giving the "very faint trace" positive. Thus, any positive result with sulfosalicylic acid denotes excess protein in the urine, if the daily urine output has been more than 1,000 ml. This test is used as the method of choice (using quantitative standards) by most life insurance companies.

King (*J. A. M. A.* 155:1023-1026 [July 17] 1954; *Ann. Int. Med.* 42:296, 1955) has reported on over 5,000 young males referred to an Army hospital because of proteinuria. Using his screening procedure of "serial urine protein excretion" over a period of 18 hours, he has concluded that continuous proteinuria indicates significant organic renal disease. Spiro (*Am. J. Path.* 35:47, 1959), utilizing the electron microscope, has shown that the structural basis for proteinuria in renal disease is the presence of gaps in the basement membrane of the glomerulus. For routine use, the need is not for a more sensitive test but rather for recognition of conditions that may cause false-positive results (e. g., with the sulfosalicylic acid test). Examples of such conditions are (1) dehydration, (2) less than 1,000 ml. urine output for the day, (3) many bacteria and/or large amounts of amorphous urates, (4) condition after use of iodine-containing drugs for [illegible] (5) condition during treat [illegible] due to the metabolite, 1-butyl-3-p-carboxyphenylsulfonylurea.

SECONDARY ADRENAL INSUFFICIENCY

To the Editor:—*What is the effect of cortisone and ACTH on atrophy or hypertrophy of the adrenals? What is the advisability of alternating ACTH with cortisone when therapy is continued for any length of time?*

C. D. Klaus, M.D., Iron Mountain, Mich.

Answer.—When ACTH is given, hyperplasia of the adrenal cortex occurs, with an extensive production of hydrocortisone in addition to small amounts of corticosterone, estrogens, and androgens. Maximal ACTH stimulation produces about 10 mg. of hydrocortisone per hour. There is only a temporary secretion of aldosterone during ACTH stimulation, after which time aldosterone secretion is independent.

If administration of ACTH is stopped suddenly, a lag phase of five to seven days' duration occurs before the pituitary-adrenal system recovers. It is during this time that the patient is in a relative state of adrenocortical insufficiency and an adrenal crisis may develop should he be subjected to stress, such as a severe infection, operation, or injury. The lag phase after ACTH therapy is much shorter than that after therapy with cortisone and its derivatives. The reason for this difference is that the corticosteroids depress the pituitary as well as the adrenal cortex. Deaths of patients have resulted when ACTH and cortisteroid therapy has been stopped abruptly during stress such as trauma, infection, or when an operation is contemplated.

When cortisone, hydrocortisone, or their derivatives are given for several weeks, the lag phase may be as long as six weeks to a year after therapy is stopped. The question often arises as to whether one encounters a permanent irreversible suppressive effect on the pituitary adrenocortical system from prolonged corticosteroid therapy. To date, there is no evidence of such an effect. Unless there has been damage to the pituitary or the adrenal cortex, the adrenal will respond to exogenous ACTH and eventually the pituitary production of ACTH will occur. The reduction of ACTH and corticosteroid therapy should be gradual and cover a period of several weeks. The last dose of corticosteroid therapy should be the morning one. There is no advantage in giving ACTH along with cortisone or its various derivatives.

EFFECT OF FOOD ON LABORATORY TESTS

To the Editor:—*May liquids or food be given to patients who are to have blood chemistry tests?*

Murray W. Shulman, M.D., Irvington, N. J.

Answer.—All physiological investigations should begin with the experimental subject under some basic conditions. In clinical practice it is difficult to satisfy such conditions, but much can be accomplished by withholding food and limiting fluids for a period of time preceding the withdrawal of blood for chemical tests. Most textbooks on clinical pathology advise such a procedure; usually blood is withdrawn before breakfast. The following quotations are examples of this restrictive imposition:

"The concentration of various constituents of the blood is materially altered for a time after meals, and it is therefore necessary, for the sake of uniform results, to obtain the blood after a twelve hour fast, that is, before food is taken in the morning" (Todd, Sanford, and Wells: Clinical Diagnosis by Laboratory Methods: Working Manual of Clinical Pathology, ed. 12, Philadelphia, W. B. Saunders Company, 1953).

"As a general rule digestion has a profound influence upon most of the chemical constituents of the blood requiring that the latter should usually be taken after a period of fasting and preferably in the morning before breakfast" (Kolmer: Clinical Diagnosis by Laboratory Examinations, ed. 2, New York, Appleton-Century-Crofts, Inc., 1949).

Besides the alteration in chemical constituents of the blood brought about by various types of food, the presence of postprandial opalescent serum is a disadvantage in performance of some procedures, such as determinations of serum bilirubin, calcium, and sulfobromophthalein levels. There also is the problem of keeping burners in flame photometers clean when any particulate or heavy lipoidal material is present. It is impracticable to attempt to control what patients may eat before a test; blood lipids are particularly susceptible to changes caused by intake of fats, and tests for glucose are affected by the ingestion of carbohydrates. Determinations of chloride, urea, nonprotein nitrogen, carbon dioxide–combining power, creatinine, and transaminase values are not particularly influenced by the ingestion of food.

In general, a procedure that calls for no food intake for 6 to 12 hours before blood is to be obtained for chemical determinations will yield results far more consistent than if food were allowed to be taken. In some instances the intake of food will result in erroneous and misleading results of such tests. For example, blood for chemical tests frequently is withdrawn at the same time that specimens of serum are taken for flocculation and complement-fixation tests and that blood is taken for the determination of hemoglobin level. Serious errors can result in the latter determination in the presence of opalescence if a photometer is used; similarly, an excess of lipids in the serum may affect serologic results.

EFFECTS OF STEROIDS ON BRAIN

To the Editor:—*Please supply any available information on effects on the central nervous system of adrenocortical steroid and related therapy.*

Roy J. Ward, M.D., Worcester, Mass.

Answer.—Clinically, large doses of ACTH, cortisone, hydrocortisone, prednisone, prednisolone, triamcinolone, and dexamethasone produce such divergent psychological reactions as euphoria, psychoses, and suicidal depressions. Rome and Braceland (*J. A. M. A.* 148:27-30 [Jan. 5] 1952) related the type of reaction to the patient's personality and found that psychotic reactions tend to occur in patients whose psychological adjustments are marginal. Psychosis is often preceded by restlessness, tension, and insomnia, which are indications for reduction of dosage, or, if this is not possible, administration of tranquilizer drugs.

This group of adrenocortical steroids is also capable of inducing convulsions, in contrast to desoxycorticosterone acetate, which is an anticonvulsant agent (McQuarrie and others: *J. Clin. Endocrinol.* 2:406, 1942; Aird and Gordan: *J. A. M. A.* 145:715-719 [March 10] 1951). Experimentally, the anti-inflammatory steroids lower the threshold to electroconvulsive shock, while desoxycorticosterone raises it (Woodbury: *Recent Prog. Hormone Res.* 10:65, 1954). Smaller replacement doses of cortisone abolish the electroencephalographic abnormalities of adrenal cortical hypofunction (Addison's disease) (Thorn and co-workers: *Tr. A. Am. Physicians* 62:233, 1949) and of congenital virilizing adrenocortical hyperplasia (Bartter and associates: *J. Clin. Invest.* 30:237, 1951).

Curiously, no alteration in cerebral metabolic pattern is found after administration of large doses of ACTH, even during ACTH-induced psychosis (Schieve and others: *J. Clin. Invest.* 30:1527, 1951), although other steroids with prominent central nervous system activity exert profound cerebral metabolic effects (Gordan: *Recent Prog. Hormone Res.* 12:153, 1956).

OPERATION IN POSTPARTUM PERIOD

To the Editor:—*Please comment on the feasibility of doing vein strippings in the immediate (e. g., three-to-four-day) postpartum period. The need for operation has been properly established. The reason for this type of management is primarily economic (to avoid another hospitalization).*

Wallace C. Ellerbroek, M.D.
Long Beach, Calif.

Answer.—This consultant knows of no large series of cases in which multiple vein ligations and stripping have been performed in the early postpartum period. Such a procedure can be safely undertaken between pregnancies or during pregnancy up to the seventh month without encountering any difficulty. In the early postpartum period the mother's glandular system, clotting mechanism, and adaption to stress are by no means restored to normal. The stress of a two-to-three-hour-long anesthesia and that of the procedure itself does not seem justified. Breast feeding would be another complication. The economic factor here would be a poor indication for performing an elective operation Emergency operations, of course, must be performed any time in the postpartum period. The risk of withholding operation in case of a ruptured viscus needs no statistical analysis. Elective operations in the immediate postpartum period, however unless a minor procedure done with use of loca anesthesia, should be postponed for at least three months after delivery.

MULTIPLE MYELOMA

To the Editor:—*Please comment on treatment for multiple myeloma in a 72-year-old man. The diagnosis has been confirmed by bone marrow study.* *James S. McBride, M.D., Indianapolis.*

Answer.—Multiple myeloma is a uniformly fata disease. There is no known cure. The average duration of life from onset of symptoms is approximately two years, although an occasional patient has survived for 5 or even 10 years. Treatment is palliative by irradiation and administration of urethane. Irradiation is used to treat any bone lesions that are symptomatic and demonstrated on skeletal survey. For its systemic effect urethane is given as follows: Start with 1 Gm. per day for two or three days, then 2 Gm. per day for two or three days, and so on until 5 Gm. per day is attained, if the patient will tolerate this large dosage. Keep up this regimen until a total of 150 Gm. has been given; then revert to a daily dose of 1 or 2 Gm., depending on the white blood cell count. If the count is about 2,000 per cubic millimeter, give 1 Gm. per day; if it is 6,000 or 7,000 per cubic millimeter, give 2 Gm. per day. This maintenance dosage is continued indefinitely, even for several years.

FISH IN LOW-FAT DIETS

To the Editor:—*Please give answers to the following questions. In the treatment of coronary artery disease, is the degree of exclusion of fish oils and fats in the diet the same as for animal fats? Would this include only the more fatty fish such as salmon, mackerel, and whitefish? In a patient on a low-fat diet, is the ingestion of small amounts (less than 2 oz. daily) of corn oil or the newer corn-oil margarines of any value? Is the ingestion of these small amounts of corn oil of any harm?*

M.D., New York.

Answer.—In the treatment of coronary artery disease with a low-fat, low-cholesterol diet, the incorporation of large amounts of fish of any kind is considered desirable and beneficial. It has been shown in clinical trials that the addition of fish and corn oil decreases serum cholesterol levels below those achieved with a low-fat, low-cholesterol diet alone. The addition of up to 2 oz. of corn oil to such a diet should be allowed only if obesity is not a problem or after weight reduction has been achieved in obese individuals. In using corn-oil margarines, only those which are not hydrogenated can be recommended. While it is advisable to use such a harmless hypocholesteremic regimen, it is only fair to state that this is on the logical assumption that lowering the blood cholesterol level will benefit clinically manifest atherosclerosis—which is as yet unproved.

NEOSTIGMINE IN ALLERGIES

To the Editor:—*What are the dangers of giving neostigmine to a patient who is known to have had allergies and/or asthma? The drug is being considered for testing a patient for myasthenia gravis and for treatment of paroxysmal auricular tachycardia.* *M.D., New York.*

Answer.—Any symptoms which would follow the administration of neostigmine to a patient who is allergic, and especially to an asthmatic, would be the result of its pharmacological action and not because of an abnormal, untoward, or allergic reaction. There is apparently no recorded case report of allergy to neostigmine. Therefore, this possibility offers no problem in the asthmatic patient. However, neostigmine may induce an attack of asthma or aggravate a previously existing one because of its pharmacological action. Neostigmine is a cholinesterase inhibitor. Given in large enough dosage, it may induce bronchospasm by allowing sufficient acetylcholine to accumulate to act on the bronchial musculature. But in testing a patient for myasthenia gravis or in treating one with paroxysmal auricular tachycardia, the dosage used probably would be insufficient to induce an asthmatic attack. Its administration in these circumstances therefore should be safe.

PRENATAL CARE AND FLUORINE

To the Editor:—*Is fluorine used in the form of sodium fluoride beneficial in the development of baby teeth in utero? Is it indicated for prenatal care?* *M.D., Massachusetts.*

Answer.—There is little evidence to suggest that low levels of fluorides can pass the placental barrier. In any case, the formation of prenatal enamel is so perfect that addition of fluoride in prenatal care is not indicated.

SURGERY OF CECAL TUMOR

To the Editor:—*A 55-year-old man was operated on for acute appendicitis and a mass was found in the base of the cecum. The differential diagnosis was carcinoma of the cecum or cecal diverticulitis. Is it possible to make the diagnosis on a gross examination? Should the cecum be opened to view the mucosa? Should an ileocolic resection be performed when the exact diagnosis is not certain? If the diagnosis is presumed to be cecal diverticulitis, what is the proper treatment?*

M.D., New York.

Answer.—It is not possible in all abdominal explorations to determine whether cecal masses are benign or malignant. The colon should not be opened for the sole purpose of viewing the mass, and the right half of the colon and terminal portion of the ileum should not be resected unless obstruction is present. In the absence of obstruction, a cecal diverticulum may be removed in a manner similar to removal of an appendix, unless it has become acutely inflamed and involves the cecum (in such cases the correct diagnosis cannot be made). The initial incision should be closed, the patient prepared with antibiotics, and a second operation performed six to seven days later. If the mass persists, a resection would be in order.

DIAGNOSIS OF HERNIA

To the Editor:—*A middle-aged man with dilated external inguinal rings has been told that he has a direct hernia. Examination shows no protrusion through the external ring, but the palpating finger can detect a definite impulse in the posterior wall of the inguinal canal. I feel that this is more or less normal for men of that age, but it has raised a point as to when a direct hernia can be classified as such.* *M.D., Pennsylvania.*

Answer.—Most writers on the subject seem to agree that a hernia must be thought of as a defect or a hole in the abdominal wall through which abdominal contents may protrude. This opening may be an abnormal one or a pathological enlargement of a normal aperture. A weak point or actual defect in the abdominal wall through which no content has as yet protruded may be thought of as a potential hernia. A definite sac is not necessary to establish existence of a hernia. In direct hernia, the fundamental cause of the hernia is a weakness of the abdominal musculature. There is a deficiency in the inguinal triangle (lower margin of the internal oblique muscle above, rectus sheath medially, and the inguinal ligament below). If such a defect is present and if a sac protrudes through this defect, the patient has a direct hernia.

CARE OF CHRONIC ULCERS

To the Editor:—*Has the following combination treatment for deep ulcers, sinus tracks, gangrenous lesions, bedsores, or other chronic lesions ever been published? 1. Apply proteolytic enzymes—combined streptokinase and streptodornase or trypsin and chymotrypsin. 2. Apply iodochlorhydroxyquin (Vioform) powder. 3. Apply granulated sugar. 4. Use dry dressing if necessary. There is rapid lysis of old debris in a few days, all infection disappears, and rapid healing occurs.* *Joe C. Gilbert, M.D., Lebanon, Pa.*

Answer.—The method submitted apparently has not been published as a combination treatment. Doubtless many superficial ulcers and sinus tracks would be benefited by such treatment. Innumerable medicaments such as the above have been used on chronic leg ulcers secondary to varicosities or thrombophlebitis without resulting in healing, however. It is the consensus of vascular surgeons that such ulcers should be widely and deeply excised, the varicosities eradicated, and the defect covered with skin grafts. Gangrene of the toes or feet secondary to marked arterial insufficiency also does not usually respond to such measures but requires some specific aid to circulation.

POSTPARTUM HAIR PROBLEMS

To the Editor:—*A postpartum patient complained at six weeks of complete loss of all curl in her hair. Previous to this pregnancy, her hair had a natural wave. A permanent wave was attempted but produced absolutely no effect. Please give information on the cause and treatment.* *Sheldon M. Biback, M.D., Seattle.*

Answer.—Women who have trouble with the hair after childbirth are usually anemic, hypoproteinemic, or both. Diffuse hair loss is common; spontaneous regrowth may be expected after a few months. A hypothyroid state may follow parturition, influencing hair nutrition, texture, and responsiveness to cosmetic physiochemical procedures. The effect of fatigue on the mother of a new baby also appertains. The measures likely to bring about a return to normal include a diet high in protein; the restriction of caffeine, because it only masks fatigue a plan for enabling the woman to secure adequat rest; the administration of a suitable hematinic; an the correction of hypothyroidism, if it is present

SAFETY OF PETROLATUM ON SKIN

To the Editor:—*Will petrolatum jelly applied t the skin daily over a protracted period of tim such as years, be harmful either as a potenti carcinogen or because of possible effects on ski glands?* *M.D., New Jersey.*

Answer.—Petrolatum, which is said to be a mi ture of semisolid hydrocarbons obtained fro petroleum, is considered by most dermatologists t be a safe base for topical application to the ski There is no good evidence that it can act as a ca cinogenic agent or as a photosensitizer or that has any of the undesirable properties of certai other hydrocarbons. It is doubtful that it coul have any adverse effects on the sebaceous or swe glands.

RADIUM ON WATCH DIALS

To the Editor:—*Is there any danger of radiati from wearing a wrist watch with illuminated di and hands?* *M.D., West Virginia.*

Answer.—Watches with luminous dials usual contain small amounts of radium painted on th dial numerals and hands. In a recent article, We ster (*Radiology* 72:493, 1959) calculates that if average watch with a luminous dial is worn co tinuously, the radiation dose to the gonads wou be 20 mr per year. While this amount of radiati is not high, it is significant. In an evaluation unnecessary exposure to radiation, the radiati from such watches must be considered.

WASHINGTON NEWS

Burney Urges Expanded Physician Supply . .
New Campaign to Diagnose Strep Infections . .
Social Security Disability Views . .
Miscellany . .

SOCIAL SECURITY DISABILITY HEARINGS BEGIN

A House Ways and Means subcommittee opened hearings on administration of the Social Security Disability benefits program, and an official of the American Medical Association offered suggestions as to possible changes in the program.

Dr. George F. Gsell, a Wichita, Kan., ophthalmologist and a member of the A. M. A.'s Committee on Medical Rating of Physical Impairment, stressed that the medical criteria used in the program are "adequate for their purposes and that administration of the program seems to be improving."

He pointed out to the subcommittee, headed by Rep. Burr Harrison (D., Va.), that he was not testifying as a representative of the A. M. A., but as a private physician.

Dr. Gsell said the two most common remarks he hears about the disability program deal with the adequacy of medical reports and delays in adjudication. "These are not separate problems, obviously the first can cause the other."

He said that in some cases physicians are required to fill out forms for former patients who then receive consultative examinations from another physician, with the former receiving no reimbursement. "The delay caused by this procedure could possibly be obviated if the attending physician were authorized to examine the applicant and be reimbursed from the trust fund for the expenses involved in 'working up' the report."

Reviewing examiners frequently are specialists in one area and may have to ask a consultative examiner for a supplemental report in these cases outside his field, the witness noted. "Possibly the establishment of a board of consultants to handle the few cases of this nature would eliminate delays."

Dr. Gsell said consultative examiners in many instances are asked to perform examinations for \$10 or \$12 for which they would normally charge \$50 or \$75. "Negotiations between constituent medical associations and state agencies are being carried out so as to provide a fair and adequate reimbursement for physicians called upon for these examinations."

As a possible solution to the occasional long delays in adjudicating cases, Dr. Gsell suggested an arbitrary period of—say 120 days—after which an applicant who has not personally caused the delay could ask the appeals board or a group established for this purpose, to adjudicate his case.

In other testimony, George K. Wyman, deputy commissioner of social security, said the department has under active consideration three legislative proposals for the disability program. These are (1) elimination of the 50-year age requirement, (2) authority to grant continuous payments to a person who has rehabilitated himself on the same basis as payments are made to a person who returns to work, i. e., payments would continue for one year after determination that the person is no longer disabled under the terms of the law, and (3) that the Bureau of Old Age and Survivors Insurance be given authority to reverse denials by the state as they have authority now to modify allowances.

Lloyd Nelson of the general accounting office said his agency had reviewed the administration of the disability program and in general believed that it was being carried out in accordance with the terms of the law, but his organization had recommended that the HEW Secretary report to Congress on the continued use of the federal-state mechanism.

RHEUMATIC FEVER PROGRAM

The government has announced the start of a national campaign for the rapid diagnosis of streptococcic infections. Disclosing the program, Arthur S. Flemming, Secretary of Health, Education, and Welfare, said that "largely because of our inability to break the 'chain reaction' in the past from such infections to rheumatic ailments, about 20,000 persons die each year from rheumatic fever and rheumatic heart disease."

A new method of detecting streptococcic infections will be used, known as the "fluorescent antibody" technique. Under it, antibodies for streptococcic germs are mixed with throat swabs; if the swabs are infected the result can be detected with ultraviolet light. The process was discovered by Dr. Albert Coons of Harvard School of Medicine in the early 1940's.

The Public Health Service, after testing 1,200 persons by the standard method and the fluorescent method in recent years, concluded that results showed the two-or-three-hour fluorescent test as accurate as the standard method, which takes several days.

Dr. James Watt, director, National Heart Institute, said laboratory personnel will have to be trained across the nation in use of the test and that this may take two or three years. PHS is training local personnel and assigning 40 PHS physicians to

(Continued on next page)

whenever
digitalis
is needed

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Lown, B., and Levine, S. A.:
Current Concepts in Digitalis Therapy, Boston,
Little, Brown & Company, 1954, p. 23, par. 2.

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meet with state and local health departments to determine the best ways to take advantage of the new test.

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SURGEON GENERAL CALLS FOR MORE PHYSICIANS

U. S. Surgeon General Leroy E. Burney declared that the "occasion for action has arrived" to take steps to increase the number of physicians in this country.

Pledging his support to the goals outlined by a special 22-member advisory committee, Dr. Burney said that "our requirements are sufficiently urgent that we must proceed toward increasing the output of physicians, even though in some details we are not yet sure what each step will be."

Referring to the study group's recommendations, which included a 10-year 500 million dollar program of federal aid for construction of medical schools, the official asserted: "I concur fully with the purposes and intent of these recommendations.

"In view of the numerous competing needs for scarce federal funds, I am not in a position to forecast what action the administration will take on the proposals involving federal legislation.

"The Department of Health, Education, and Welfare is presently engaged in the development of its legislative program for the forthcoming session of Congress. However, I can assure you that the consultant's report and recommendations are receiving serious and sympathetic consideration by our Secretary of Health, Education, and Welfare."

Dr. Burney previously said that he personally agreed with the legislative proposals. He pointed out that the administration has twice proposed legislation authorizing federal grants for the construction of medical and dental school facilities.

He made the statements in a speech before the Association of American Medical Colleges in Chicago shortly after the advisory group's 95-page report was made public. In the report, the group said there was an urgent need for 3,000 more physicians a year by the year 1975 and that present plans for expansion would not be enough to meet this need.

"We must face up to the fact," said Dr. Burney, "that the situation is going to get worse before the recommendations of the consultants has been put into effect. The present ratio of physicians to population (about 1 to 740) will have dropped significantly long before we succeed in sustaining the minimum essential. In order to reach the goal in 1975, every one of the new schools recommended by the consultants must have their doors open by 1971. The 50% increase in medical school output proposed by the consultants will meet the nation's needs only if significant new ways are developed to conserve the energy and skills of the physicians in all types of medical practice."

Dr. Burney cautioned against "a hasty or ill-advised expansion of medical education facilities." He said "the point which must be emphasized here is that the medical school must be kept whole; sound in each of its three functional elements—teaching, study, and practice. . . . The larger field of medicine as a whole—medical education, medical research, medical practice—cannot long function, or even survive without them."

MISCELLANY

A conference between the Disaster Medical Care Committee of the American Medical Association and the Division of Health Mobilization of the U. S. Public Health Service resulted in general agreement that emergency life saving training would be useful to the individual in his normal daily living, would increase the nation's health manpower resources, and would, in itself, provide a deterrent to all-out war.

HEW Secretary Flemming criticized "degree mills" that offer spurious degrees through correspondence courses. Among institutions criticized were one that offered a Doctor of Metaphysics degree (Ms.D.) for courses in metaphysical healing and another that purportedly granted "Doctorates in Chiropractic, Naturopathy, Eclectic, Naturatrics, and Philosophy." Federal supervision of the mails and false advertising are ways the government can curb abuses in degrees.

The Food and Drug Administration warned against "wild claims" about products purporting to be sources of vitamin E. Since the daily diet provides more than adequate amounts of vitamin E for the average person, the FDA said, supplementing it with the vitamin isn't necessary.

The number of persons detained for medical observation in ports of entry to the United States increased more than 400% in the fiscal year that ended July 1, a total of 607 compared with only 124 the previous year. Major cause was a smallpox outbreak in Germany. More than 117,000 travelers were allowed to proceed to their destinations under medical observation requirements, a 100% jump from the 58,083 of the previous fiscal period. Most of these persons came from areas where there were occurrences of smallpox and yellow fever.

FDA officials seized 346 tons of unfit food during September, including insect-contaminated peaunts, egg noodles, and prepared baking mixes and spoiled salad dressings and lobster tails. Ten tons of tomato paste were found to contain fly eggs and maggots.

FDA officers seized 37,800 tablets of "Dynamol," a vitamin product labeled as "an adequate cure and treatment for all vitamin and mineral deficiencies." The federal agency said that in addition to caffeine, the product contained no vitamin A or D and "nutritionally insignificant" amounts of calcium and phosphorous.

Robert A. Forsythe and Dr. Winchell McKendree Craig were named to HEW posts. Forsythe, former administrative assistant to former Sen. Edward Thye (R., Minn), succeeds Elliot L. Richardson as assistant secretary for legislation. Dr. Craig was sworn in as special assistant for Health and Medical Affairs, replacing Dr. Aims C. McGuiness, who resigned recently.

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MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10, Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 *Clinical Meeting, Denver*, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

November

Academy of Medicine of Cleveland Seminar on Recent Advances in Diagnosis and Therapy of Malignant Disease, Cleveland, Nov. 18-19. Dr. H. S. Van Ordstrand, 2009 Adelbert Rd., Cleveland 6, Chairman.

American Academy for Cerebral Palsy, Statler Hilton Hotel, Los Angeles, Nov. 30-Dec. 2. Dr. Glidden L. Brooks, Brown University, Providence 12, R. I., Secretary.

American College of Chest Physicians, Dallas, Texas, Nov. 29-30. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Secretary.

American Medical Women's Association, Arlington Hotel, Hot Springs, Ark., Nov. 12-15. Mrs. Lillian T. Majally, 1790 Broadway, New York 19, Executive Secretary.

District of Columbia, Medical Society of, Statler-Hilton Hotel, Washington, D. C., Nov. 23-25. Mr. Theodore Wiprud, 1718 M Street, N. W., Washington 6, D. C.

Gerontological Society, Inc., Statler Hotel, Detroit, Nov. 12-14. Mrs. Marjorie Adler, 660 S. Kingshighway Blvd., St. Louis 10, Administrative Secretary.

International College of Surgeons, Second Western Regional Meeting, Stardust Hotel, Las Vegas, Nev., Nov. 22-24. Dr. F. M. Turnbull Jr., 1930 Wilshire Blvd., Los Angeles 57, Secretary-Treasurer.

Inter-Society Cytology Council, Statler-Hilton Hotel, Detroit, Nov. 19-21. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secretary-Treasurer.

National Society for Crippled Children and Adults, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

Puerto Rico Medical Association, Santurce, Nov. 24-28. Mr. J. A. Sanchez, Box 9111, Santurce 29, Puerto Rico, Executive Secretary.

Radiological Society of North America, Inc., Palmer House, Chicago, Nov. 15-20. Dr. Donald S. Childs, 713 E. Genesee St., Syracuse 2, N. Y., Secretary-Treasurer.

San Diego Academy of General Practice, Hotel Riviera, Las Vegas, Nev., Nov. 12-14. For information write: Dr. Harold Peterson, 5950 El Cajon Blvd., San Diego 15, Calif.

Southern Medical Association, Atlanta, Nov. 16-19. Mr. V. O. Foster, 2601 Highland Ave., Birmingham 5, Ala., Executive Secretary-Treasurer.

Southern Thoracic Surgical Association, Edgewater Gulf Hotel, Edgewater Park, Miss., Nov. 19-21. Dr. Hawley H. Seiler, 517 Bayshore Blvd., Tampa 6, Fla., Secretary.

Western Surgical Association, The Broadmoor, Colorado Springs, Colo., Nov. 19-21. Dr. John T. Reynolds, 612 N. Michigan Ave., Chicago 11, Secretary.

December

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bldg., Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York City, Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, Secretary.

American Rheumatism Association, Henry Ford Hospital, Detroit, Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

First Annual Graduate Medical Education Conference-Residency Training Program, Univ. of Pennsylvania, Philadelphia, Dec. 3-4. Dr. Alfred S. Frobese, Graduate School of Medicine, U. of Pennsylvania, Philadelphia 3, Chairman.

Medical Society of the United States & Mexico, *Valley* Ho Hotel, Scottsdale, Ariz., Dec. 2-4 (followed by two-day session Desert Inn, Las Vegas, Nev.). Dr. A. H. Tallakson, 2025 N. Central Ave., Phoenix, Ariz., Convention Co-Chairman.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly *in Anesthesiology*, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer Hous Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3 Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunder 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefis Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairma

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. Joh R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 2 30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Executi Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. D Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secretar

Western Society for Clinical Research, Carmel-by-the-Sea, Cali Jan. 28-30. Dr. William N. Valentine, U. of California Medical Cente Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. Geor Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg In Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Med cine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harbo Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tow Minneapolis 2, Executive Vice-President.

American College of Radiology, *Roosevelt Hotel, New Orleans*, Fe 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Executi Director.

American College of Surgeons, Sectional Meeting for Surgeons a Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information wri Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chica Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York Executive Secretary.

California Medical Association, Ambassador Hotel, Los Angeles, F 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Execut Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18- Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Cana Secretary.

Congress on Medical Education and Licensure, Palmer House, C cago, Feb. 7-9. For information write: Council on Medical Educat and Hospitals, American Medical Association, 535 N. Dearborn Chicago 10.

National Association of Methodist Hospitals and Homes, Desh Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, 7 Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern Califor Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), University Texas, Houston, Feb. 25-27. For information write: University of Te M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville Ho Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chica Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secreta Treasurer.

American Academy of General Practice, Philadelphia, Mar. 19- Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, M Executive Director.

American Association for the History of Medicine, Inc., Charlest S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Instituti Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadmo Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H. Saunders, *40 E. Erie St., Chicago 11.*

American College of Surgeons, Sectional Meeting, Sheraton-Portla Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H. Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, N Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ. Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., *Secretary-Treasu*

American Laryngological Association, Deauville Hotel, Miami Bea Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Te nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Socie Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. *Dr. C.* Stew Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., *Secretary.*

American Otological Society, Deauville Hotel, Miami Beach, Fl Mar. 13-14. Dr. Lawrence R. Boies, University *Hospital*, Minneap 14, Minn., Executive Secretary-Treasurer.

American Otorhinologic Society for Plastic Surgery, Inc., Deauv Hotel, Miami Beach, Fla., Mar. 6-13. Dr. Joseph G. Gilbert, 75 Barbe Lane, Roslyn Heights, N. Y., Secretary.

American Psychosomatic Society, Sheraton-Mount Royal Hotel, Mo real, Mar. 26-27. Miss Joan K. Erpf, 265 Nassau Rd., Roosevelt, N. Executive Assistant.

(Continued on page 30)

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THE FAMILY PHYSICIAN, THE GENERAL PRACTITIONER, AND THE INTERNIST

E. Grey Dimond, M.D., Kansas City, Kan.

A program to train students for practice as family physicians must satisfy certain stringent requirements. The family physician's practice is not limited to internal medicine, and his training must be much broader. It must provide experience in obstetrics, pediatrics, and psychiatry. It must prepare him to deal with emergencies in a way that will facilitate, not hamper, the subsequent work of the specialist. The program wherever instituted must have an adequate administrative framework. It should lead to certification and should offer the physician an opportunity to achieve status, honor, and recognition not only before the laity but before the eyes of his professional colleagues. This can be achieved by replacing the present 12-month internship with a 24-month program based on internal medicine but broadened to give the necessary range of experience.

IN a previous article[1] I attempted to develop the reasoning behind my belief that the ambitions of those seeking identity and training as general practitioners and the ideals of those claiming the role of family physician for the internist were actually one and the same. In this present article it is not necessary to repeat my reasoning, and anyone interested in the background leading up to this present paper is encouraged to read the other paper. The two articles represent a continuing thought.

Stated briefly, a basic problem seems to be present in the American medical education scheme: the present graduate, although duly licensed and therefore legally identified as a "physician and surgeon," is not in reality prepared for the role of "general practitioner" or "family physician." Special committees of the American Academy of General Practice and of the American Medical Association have been at work, attempting to define first a family physician, second what his "privileges" (surgery? obstetrics?) should be, and finally what training program is necessary to create this product.

Primarily at the behest of the American Academy of General Practice a host of general practice residencies were established after World War II. These have as a group been unsuccessful (with certain excellent exceptions). Further pressure by the Academy of General Practice has been directed toward urging the establishment of departments of general practice in medical schools. This idea has met with a cool reception from medical school faculties.

Professor and Chairman, Department of Medicine, University of Kansas Medical Center.

In response to these two previous comments, first the unsatisfactory results of general practice residencies and second the antipathy of medical school faculties to departments of general practice, one might challenge me and say, "Yes! That is exactly the problem. The professors in the ivory towers are defending their specialty citadels, handling patients and their diseases piecemeal, and wilfully preventing the training of true general practitioners."

Not pretending to speak for academic medicine, but speaking for myself as a practitioner and teacher, I would rebut this challenge by saying, "If your definition of a general practitioner includes the right and privilege to dispense all forms of medical, surgical, and obstetric care, then I am not in sympathy with any present program claiming to give a man this degree of proficiency." (Again, for the purpose of brevity, I refer the reader to my previous article.[1] There I attempted to spell out my reasoning.) If we are agreeing that a degree of restriction is necessary and that the health of the American public can best be tended by making our basic medical school product a family physician, a personal physician, then we can quickly establish a mutual goal. Further, if the proponents of the academy and of the general practitioner would agree that family practice is that aspect of medical care performed by the doctor of medicine who assumes comprehensive and continuing responsibility for the patient and his family, regardless of age, then there is perhaps a readily available solution.

Proposal for the Family Physician

I have indicated above that medical school faculties have not adapted well to the idea of departments of general practice. The administrative framework of a medical school is developed on a specialty structure, because in the minds of most this best serves as a workable administrative unit, a useful teaching unit, and a superb patient-care unit. The criticism, often expressed, that the patient is treated by fragments and not as a whole in this atmosphere is simply an unreal appraisal.

The present internal medicine residency programs, with an internship and three years of residency, produce physicians who are almost perfectly trained for the role of "family physician." I have inserted the word "almost" because the present-day residency program in internal medicine, in many ways, trains the man too narrowly. He acquires a high order of ability to think in terms of physiological medicine and to balance this with an understanding of the human being. In full urban life, or large clinic life, the internist represents the best concept of a personal physician. However, he is too finely trained. His role as a family physician is weakened and his usefulness materially lessened by his relatively inadequate training in care of newborn infants, prenatal care, emergency and traumatic surgery, medical gynecology, physical medicine, and general problems of the eyes, ears, and skin. I appreciate that varying residencies in internal medicine will in varying degrees offer training in these areas; however, my general proposition, that the present-day internist is not well trained in problems of pediatrics, gynecology, and other fields mentioned above, seems a sound premise.

I reiterate: 1. The American public's best interest, from the standpoint of medicine, will be served if the basic unit of our medical structure is a personal, family physician. 2. The family physician must be able to give medical care to all family members regardless of age—must be prepared to minister to a patient in normal labor, care safely for an emergency, perform traumatic surgery, recognize surgical and subspecialty problems, and integrate the indicated specialist into the management. 3. The present graduate of our medical schools, following an internship, does not measure up to this need. 4. The training program of internal medicine prepares a man well for this role but in certain areas offers too restrictive a program. 5. The family physician must have status, honor, and recognition not only before the laity but before the eyes of his professional colleagues.

I have added item 5 because this has been a primary, although often not expressed, factor in the unwillingness of medical schools to set up general practice programs, on the one hand, and the militancy of the Academy of General Practice on the other. The image of the "general practitioner," as stated by his proponents, has not in major ways agreed with the daily observations of many, in and out of the medical schools. The need for "status" is a simple, basic, understandable urge, but the role claimed for the general practitioner by some has exceeded the true dimensions, in the experience of some critics.

If there is a real need for family practitioners, a very reasonable query would be to ask why the general practice residency programs have not succeeded. I think the generally poor long-term performance of the general practice residencies can be explained in basic terms of morale, prestige, and purpose.

First, the administrative unit of a teaching hospital does not provide an "identification" for a general practice residency. The program "belongs" to no department. No senior administrative figure controls the program. The very nature of such a residency cuts across departmental lines, and in so doing does not gain the vigor and strength of any single major department. The administration of the program is usually the duty of a committee (a synonym for lack of administration), or, even more futilely, an unfortunate young general practitioner attempts, as a part-time responsibility, to guide the program without offending the various departmental empires.

The resident participant in such a program loses the very real and significant value of "belonging" to an established, authentic department. This isolation and separateness is a true deterrent, which, along with the problems of administration, makes the general practice residency impotent.

Further, the value of Board certification is readily apparent to the young physician. The *premium* value of certification relative to the military, the Veterans Administration, and clinical groups is common knowledge. Therefore, the young man who is *considering postgraduate training prefers to invest* these years toward Board credit.

These three weaknesses of the present attempts at training a family physician can be simply summarized by stating that the general practice programs lack appeal, prestige, the significant value of certification, and, finally, an administrative framework.

Solution

Solutions to these problems might be gained by a program, offered by medical schools and at central teaching hospitals, modeled on these concepts: After graduation from medical school, a 24-month training program in family practice should be offered (see figure).

MONTH

Service	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24
2 Men	D	D	D	A	G	G	G	G	G	H	H	H	A	B	C	I	I	I	E	E	F	J	J	J
2 Men	H	H	H	B	C	A	D	D	D	G	G	G	G	G	A	E	E	F	I	I	I	J	J	J
2 Men	G	G	G	G	G	A	H	H	H	D	D	D	B	A	C	I	I	I	J	J	J	E	E	F

CODE

A. Emergency Room

B. X ray

C. Physical Medicine

D. Pediatrics Ward

E. Pediatrics Out Patient Clinic

F. Pediatric Newborn Service

G. Clinics (see next graph)

H. Medicine Ward Service

I. Medicine Ward Service

J. Medicine Ward Service

K. Obstetrics. For physicians desiring further experience the second 3 months on Medicine (Code I) will be substituted by Obstetrics.

DETAILS OF CODE G

G. Clinics (5 months)

	Mornings	Afternoons
M	ENT Clinic	Psychiatry
T	Eye Clinic	Medical GYN Clinic
W	Allergy Clinic	Dermatology Clinic
T	Prenatal Clinic	Medical GYN Clinic
F	Proctoscopy	Psychiatry (next graph)
S	Pediatric Heart Clinic CPC	

DETAILS OF PSYCHIATRY

The two afternoons each week in Psychiatry will continue throughout a 15 month period and will be outpatient experiences.

NIGHT CALL

Regular Night Call responsibility will be followed while on Code D, E, H, I, J.

Emergency Room Night Call will be followed while on Code A, B, C.

Schematic representation of two-year program in internal medicine in preparation for family practice.

It must be a program which will satisfy certain stringent requirements, such as making full use of the present administrative structure of a medical school as a logical extension of the department of internal medicine, so as not to add new burdens to the curriculum but instead use existing effort. The program must also provide experience in psychiatry, *to prepare for continuing experience at an office* level. It should provide an increasing responsibility in the practice of broad general medicine, perhaps in a nine-month program divided into three-month *increments of increasing responsibility, and in pediatrics*, in the ward and clinic (general pediatrics), and in care of newborn infants. Full experience with problems of trauma and emergency nature could be got in 60 days and 40 nights of emergency-room duty. Opportunity for experience in obstetrics would be elective and, if chosen, relative to the student's experience. Experience with office manifestations of specific organ diseases, such as those of the eye, ear, nose, throat, and skin; allergies; disease of the rectum; prenatal complications; medical gynecology; and pediatric heart disease, as well as experience with possibilities of physical medicine and rehabilitation, would be included. Finally, some experience with radiology—the role of atomic medicine, safety problems, interpretation of films, and the adequate preparation of patient—is necessary. The program must be acceptable as graduate training by other Boards. During the entire period the physician would function as a resident in medicine, responsible to the department head and participating in all administrative functions of the department of medicine.

This two-year program would be the basic, initial training program for all men preparing for certification in internal medicine. At the conclusion of this initial two years an examination would be given by the American Board of Internal Medicine. This examination might be designated part 1, and on completion the graduate would be identified as a diplomate in family practice of the American Board of Internal Medicine. If the diplomate elects to go ahead with part 2 of his internal medicine board examination, a further two years of training would be required, leading to examination with certification as a diplomate in internal medicine.

But if, instead, he elects to follow a subspecialty area of internal medicine, such as cardiology or gastroenterology, this second two-year period could be in a restricted area with final certification by examination by the particular subspecialty Board. Other Boards should be approached and their approval gained for the initial 24-month training program applicable toward their respective certification. Obviously, the American Board of Internal Medicine would be the key to the acceptability of such a program and a proper initial approach to the Board would be essential.

Such a program resolves the criticisms I have cited and also serves to eliminate the present weaknesses in the internship. By present weaknesses I refer to the fact that our 1959 graduates are having major clinical experiences in medical school, and the general rotating internship no longer serves its original purpose. In practice, the internship today has become a period of "academic let-down" and only infrequently continues the growth of the student at the junior and senior pace. Today's graduate has had bedside clinical experiences for at least two years and his level of practical experience eliminates the original purpose of the internship. Today's graduate has a considerable background in obstetrics and in general is well prepared to assist normal labor. The rapid improvement of medical school curriculums has simply pre-empted the original role of the intern.

A program such as this would effectively bring the medical schools, their teaching beds, and their departmental administrative staffs into this field. The real need for a physician who can function as a true family physician is already upon us. The Academy of General Practice has rightfully insisted that academic medicine recognize this need. The finished product of the present training in internal medicine is, by exclusion, not prepared in the specific fields of prenatal care, care of newborn infants, medical gynecology, and emergency and traumatic problems—however, the department of medicine is the logical administrative unit and the American Board of Internal Medicine is the logical certifying unit.

Our present medical school graduates leave school with a high level of experience compared to the graduates of 15 years ago. The present 12-month internship represents a poor utilization of time. A 24-month program, based on internal medicine and broadened as described in the figure, would, in series with the medical school preparation, result in a product which could rightfully be labeled family practitioner.

The American College of Physicians is the logical group with whom the family practitioner should identify. This honor, with the associated Board certification, will bring the family physician into the honored circle which he seeks, needs, and deserves.

Reference

1. Dimond, E. G.: Generalist and Internist, J. A. M. A. **164:**1306-1309 (July 20) 1957.

ATTITUDES TOWARD THE HANDICAPPED.—As a group parents fear a child's becoming disabled. A mother feels instant relief at learning a newborn child is physically whole, while a sense of guilt is evoked by presence of a handicap. Parents are hesitant to allow the handicapped child to associate with those who are not. Unconscious beliefs that disability is contagious increase the social isolation of the handicapped child. . . . Awareness that disability can happen without parental fault will permit parents to accept disabled children and allow the nonhandicapped to associate freely with the handicapped. A positive social climate can do much to eliminate restrictions placed on the disabled and alleviate the problems of discrimination. If those of us in rehabilitation would add, to knowledge and skill, sensitive understanding of man's common humanity, our professional attitudes would reflect empathy rather than sympathy, respect rather than tolerance, and acceptance rather than pity. William Gellman, Ph.D. (Jewish Vocational Service), Roots of Prejudice Against the Handicapped, *Rehabilitation Literature,* June, 1959.

CAREER-RELEVANT VALUES OF MEDICAL STUDENTS—A RESEARCH NOTE

Lathrop V. Beale, M.A.
and
Louis Kriesberg, Ph.D., Chicago

Concern with changes in career-relevant values of medical students as they progress through school sometimes turns attention away from commonly held values which do not change although less common values become somewhat more important. A recent survey conducted by the National Opinion Research Center provides data which can be used to study changes in both kinds of values among medical students.

The survey was conducted in the spring of 1956; 1,086 male medical students in 44 medical schools were interviewed. A sample of accredited schools was drawn after the schools had been stratified by major census region and public-private financing; student names were then drawn at random in each school. Interviews were completed with 97.5% of the students in the sample. The survey was conducted to gather information relevant to the Army Medical Service's efforts to recruit junior medical officers and was supported by the Research and Development Division, Office of the Surgeon General, Department of the Army. The extensive findings have been reported by Cahalan and Collette,[1] and a summary of some of the findings has been given by Cahalan, Collette, and Hilmar.[2] This secondary analysis was done incidentally to research planning undertaken at the instance of and with contract funds provided by the National Institutes of Health.

A representative sample of students in 44 approved medical schools in the United States were asked to evaluate the importance of several considerations in deciding on the kind of careers they would prefer. The form of the question was as follows: "I'd like to know how important certain considerations will be to you personally in deciding on the kind of medical career you would like to have. Would you say that . . . would be: very important, fairly important, or not at all important?" Of the considerations the students were asked to evaluate, three deal with the central part of the doctor's role, his contacts with patients; two deal with the intraprofessional part of his role, his relationships with colleagues; and two deal with individual matters of medicine as an occupation. In the order named the items are as follows: (1) having the opportunity to know your patients well, meeting particularly challenging diagnostic problems, and having patients who will appreciate your efforts; (2) having enjoyable relationships with colleagues, and having prestige within the medical profession; and (3) being able to establish your own hours of work, and making a good income.

Student ratings of the last two items suggest that students become more concerned with matters extrinsic to medical practice as they move through their medical school training. (These data deal with different students in each year of medical school, not with a panel followed through its medical school career. However, the drop-out from medical schools is so low that there is only slight danger in concluding that differences between successive classes probably reflect changes in the attributes of students as they move from one school year to the next.) As the table shows, the percentage of students who think that making a good income is very important rises in successive school years. The survey also indicates that the percentage who feel that being able to establish their own hours of work is very important also rises, going from 12% of the freshmen to 21% of the seniors.

Taken alone these data suggest that medical students become more concerned with their occupational self-interest as they move through their medical training. The impression is strengthened when one looks at the year-by-year increase in the percentage of students who say that having prestige within the medical profession is very important, a change from 22% of the freshmen to 36% of the seniors. However, the percentage of students who feel that income, control over hours, and professional prestige are very important is always a minority. In each school year the considerable majority hold that income, hours, and prestige are of only fairly great importance in their career preferences.

In the area of intraprofessional relationships, students in all years put a higher valuation on pleasant relationships with their future colleagues than they do on having prestige in the profession. From 64 to 72% of the students always agree that having pleasant relationships with colleagues is very important, whereas, at the most, 36% feel that prestige is very important.

In each school year the students are rather evenly divided on the question of whether it is very important to have patients who will appreciate their

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From the National Opinion Research Center, University of Chicago.

efforts. Slightly increasing percentages, from 50% of the freshmen to 58% of the seniors, think that it is very important.

A similar division of opinion occurs in another national sample of medical students. They were asked a question phrased in personal versus professional terms: Would you prefer a patient who wants to know you only on a doctor-patient basis or a patient who wants to know you also on a friend-to-friend basis? The year-by-year differences are slight, with the following proportions who prefer a patient who wants to know them on a friend-to-friend basis: freshmen, 58%; sophomores, 57%; juniors, 62%; and seniors, 49%.[3]

When one turns from the way in which the students want patients to behave toward them to the way they, as doctors, expect to behave toward patients, the even split of opinion disappears and a strong majority opinion emerges. About three-quarters of the students in each school year say that having the opportunity to know their patients well will be an important consideration in their career preferences. Seventy-two per cent of the preclinical students and 64% of the clinical students say that meeting particularly challenging diagnostic problems will be very important.

Importance of Making a Good Income, Valuation by Year in Medical School

	Freshmen, %	Sophomores, %	Juniors, %	Seniors, %
Very important	11	13	17	21
Fairly important	79	77	78	75
Not at all important	10	10	5	4
No opinion and no answer	0	*	0	0
Total no. queried	286	280	271	249

* Less than 0.5%.

In making their evaluations practically all of the students were apparently thinking in terms of a medical career which involves constant contact with patients. Only 5% said that they would prefer to devote their main career to working with medical problems that do not require frequent contacts with patients, and only 4% were uncertain of their preference, while 91% preferred to work directly with patients most of the time. Furthermore, preference for frequent contact with patients does not seem to change in the course of medical school training; the distributions of preferences do not vary more than 4% among the students in different years of medical school.

Taken together, the students' evaluations indicate that a majority of students in each year of medical training feel that their professional dealings with their patients and friendly relationships with colleagues are of first importance as bases of career preferences. Control over working hours, making a good income, and having professional prestige consistently hold a place of lesser importance for most students.

Several recent studies[4] of medical students have dealt with the apparent decrease in idealism as students go through their medical school training. In a longitudinal study of the students at an Eastern university medical school Eron[4a] found that the mean score on his cynicism scale was significantly higher among seniors than it was among the same students as freshmen. On his humanitarianism scale the mean freshman and senior scores were similar but the number of students who scored lower as seniors was twice that of those who scored higher as seniors.

Becker and Geer[4b] find that the students' cynical expressions relate primarily to the situation of students in medical school and not to medical practice. The students whom they observed retained many of the ideals of medical practice with which they had entered medical school but apparently postponed the time to which they considered them to apply. In addition they acquired "professional idealism," the intention to live up to the ideas of practice which they had learned in medical school even though they know that most doctors do not have time to do so.

The findings of this secondary analysis suggest that some of the apparent decline in idealism may come from the year-by-year increase in the proportion of students who consider that a good income, control over working hours, and prestige are very important. The increase in the size of the minority in the extreme category may obscure the fact that a considerable majority of students in each school year evaluate these matters as no more than fairly important.

5736 S. Woodlawn Ave. (Miss Beale).

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USE OF PRIVATE MEDICAL PATIENTS FOR TEACHING PURPOSES IN THE COMMUNITY HOSPITAL

Paul W. Weld, M.D.
and
Leonard Horn, M.D., Rochester, N. Y.

With the increased medical insurance coverage of the average American family, the teaching or "staff" case has become so scarce that in recent years medical educators have had to think in terms of utilization of private patients for teaching purposes. The present paper is a brief outline of the success that the medical service of the Rochester General Hospital has had in using private patients for intern and medical resident teaching during the past three years (1956-1959).

The Hospital

The Rochester General Hospital is a 417-bed, nonprofit, community hospital which is affiliated with the University of Rochester School of Medicine and Dentistry and Strong Memorial Hospital. It consists of two divisions, the Westside Division, located near the heart of Rochester, and a Northside Division, located near the northeast periphery of the city. The medical service has a total bed capacity of 103, of which 68 are located at the Westside Division and 35 at the Northside Division. Since the emergency department is located in the Northside Division, the medical cases there tend to be of the more acute type, while those at the Westside Division are more in the area of difficult therapeutic or diagnostic problems. Optimally, there are 6 medical interns and 10 residents. This number includes a resident covering the hematology service and one the cardiopulmonary laboratory.

Evolution of the Teaching Program

In 1953 it became evident to the medical service of the Rochester General Hospital that private patients had to be utilized for teaching purposes in order to maintain the volume of teaching material available to the intern and resident staff. This preceded by two years the appointment of a full-time physician to be director of medical education in 1955. At this time, a philosophical change had to occur in the minds of the attending staff in order to allow, for the first time, another physician, the director of medical education, to make rounds on their private patients. In the beginning, a small amount of resistance was manifest, which soon abated when the great benefit to the house staff and improved patient medical care became evident to all. At the present time, the director of medical education is head of the department of education and holds a seat on the medical board of the hospital. In a teaching capacity, since he is a board-certified internist, he sees problems regularly on the medical service and coordinates teaching on the other services. It should be noted that the function of the director of medical education is not limited to house staff education. For example, in 1958, a seminar on medical education was conducted for the chiefs of services by a group of specialists in education from a nearby city.

Private Rounds

In 1956, after much controversy, private rounds by an attending physician twice weekly on each private medical floor became a reality. Each month four attending physicians are assigned to rounds, two on staff and two in private medicine. These assignments, made by the chief of medicine, are according to the teaching ability and professional qualifications of the physicians. Rounds are conducted twice weekly on the private floors and three times weekly on the staff floors. At the start of this program, the proviso was added that any physician desiring it could write in the order book that his patient should not be used for teaching purposes. It is interesting that on no occasion during the three-year period has this privilege been used. In reality, it can be said that virtually every private patient has been a teaching case over this three-year period, and the results of a recent house-staff questionnaire indicate that, in all instances, teaching on the private floors has been equally as successful as that in which staff patients were used. The "rounding" on the private floors either follows the plan of observation of a single interesting problem case with detailed discussion after the bedside presentation and examination or of the more conventional rounding exercise with several patients being seen during the course of the rounds. If, in the discussion, certain diagnostic or therapeutic suggestions are thought to be indicated, these are subsequently brought to the attention of the private physician by the interns. The duration of the rounding exercise has been on an average of one and one-half to two hours.

Patient Reaction

Almost universally, patients have been eager to be seen on teaching rounds, and some have expressed their favor at having what amounts to a

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Director of Medical Education, the Rochester General Hospital, and Clinical Instructor in Medicine, University of Rochester School of Medicine and Dentistry (Dr. Weld) and Chief of Medicine, the Rochester General Hospital, and Clinical Assistant Professor of Medicine, University of Rochester School of Medicine and Dentistry (Dr. Horn).

consultation at no added expense. If a patient desires to have no rounding conducted, he has the privilege of asking his physician to write "no rounding" in the order book. The favorable patient reaction has indeed been most gratifying to the original proponents of this teaching program.

Staff Reaction

Of major significance and great interest is the fact that the few physicians who reacted most strongly against the starting of such a rounding program are now among its heartiest proponents. Many physicians feel that the community health of Rochester has improved with this program, since in many instances difficult medical problems have the benefit of another physician's thinking. Though slightly fewer medical consultations have been held, this has not resulted in any major change in the consultation service per se and has created no animosity on the part of the physicians rendering this type of service. This may in part be due to the fact that most of the rounding physicians are the ones most likely to be chosen for consultation purposes, since training and experience are major factors in the choice of a good rounding physician. There has actually resulted, since the advent of this program, an increased number of consultations from other services.

Summary

Every hospital is a potential teaching institution. In this day, with the diminishing number of staff or ward patients available, many hospitals find that they must use private patients for teaching purposes. The experience in the utilization of private patients in teaching at the Rochester General Hospital for three years has been extremely gratifying.

1425 Portland Ave. (21) (Dr. Weld).

DECLINE IN QUALITY OF MEDICAL TEACHING

Maurice B. Visscher, Ph.D., M.D., Minneapolis

The Second World Conference on Medical Education, sponsored by several organizations including the American Medical Association and held in Chicago, Aug. 30 to Sept. 4, 1959, focused part of its attention on the problem of recruiting, training, and retaining talent in medical education. It is not surprising, perhaps, that the conferees from the industrially underdeveloped countries such as India and Indonesia should report that in their countries the salary scales for teachers are so low that recruitment of able persons for full-time teaching and research in the basic medical sciences is extremely difficult, or even impossible. In fact, a former officer of the World Medical Association from India stated that in his country it was virtually only those persons who could not succeed in the practice of medicine who became teachers, quoting the old saw, "he who can, does. He who cannot, teaches."

Oddly enough, the situation in the richest country in the world, the United States, is acquiring sufficient resemblance to that in the poorest countries to warrant serious consideration. The parts of the world in which there is the greatest real competition for academic posts are the moderately wealthy regions such as Scandinavia, Switzerland, Belgium, Germany, Holland, and the United Kingdom.

The conferees from the United States were in agreement that a serious shortage exists in the supply of preclinical medical science teachers. Scores of budgeted vacancies in basic science departments exist in U. S. medical schools. Furthermore, actual vacancies tell only a small part of the story, because in most instances, when a position cannot be filled with a candidate of caliber, the institution lowers its sights and appoints someone of less than optimal ability and training. In fact, it is this practice that is most damaging to medical education and to the ultimate public interest.

The fact that the American culture has not, in spite of the many hundreds of millions of dollars used annually in medical teaching and research, been able to make academic careers in the basic medical sciences as attractive as they are in the less wealthy but culturally more mature countries of the world is disturbing as far as the future of medicine is concerned. It is unrealistic to suppose that, in general, high-grade products are going to come out of schools with inferior teachers. The very immensity of the annual investment in medical teaching and research demands that every effort be made to make that investment productive. It could become a national scandal if these hundreds of millions of dollars annually were to be wasted in part by having less than the most competent teachers and researchers control the expenditure.

Professor and Head of the Department of Physiology, University of Minnesota.

Many factors enter into the situation which exists in the United States on this score. A superficial analysis might lay almost all of the blame on the relatively low salaries in academic careers. This is unquestionably a large factor, but it is not the whole difficulty. Another major factor is the low social prestige of the teaching profession as a whole in the United States. This in turn is again partly a result of the low economic rewards in a culture in which dollars are much more the yardstick of success than is the case in European cultures. Still another discouragement to young medical students against entrance into academic careers is the inadequacy of their basic science and mathematical training in high schools and colleges. They see a long, hard road ahead of them if they choose such careers.

Also, lowering of the average age at marriage means that most medical graduates now have a minimum of two mouths to feed. They also face the necessity of spending time with their wives and children which, if they were single, could go into study.

The net result of all these factors is that basic medical science in the United States is in danger of serious deterioration in quality. The expansion of the total educational enterprise is, if anything, making it worse rather than better, because the dilution with less than first-rate scholars will be progressive. The government, the foundations, the universities, the medical profession, and especially the public—all have a vital stake in the matter. Each of these agents already has taken some cognizance of the facts, but adequate solutions are not yet in sight. Universities are raising salaries, but salaries for most basic science teachers are still far below levels at which a university professor could send three or four children through college without dissipating his lifetime savings. Foundations are making contributions to the training of recruits, as is the government. The latter two are also making almost unbelievably large sums of money available to support research. Actually, it is open to question whether in the long run it would not be preferable to put significant fractions of this support for research into making research and teaching careers more attractive, so that competent persons will become the medical scientists of the future.

As a working medical educator I have seen in recent years, that is, since the inflation after the Korean war, a definite change in the caliber of students who consider entering academic careers. In the department in which I have worked for 20-odd years, the fraction of applicants for graduate work which we are obliged to turn down has increased greatly, and not because our requirements have been raised. Today, many more of our applicants come from the "disappointed premed" group and others from the lower fraction of medical school classes. Fortunately, we do, to be sure, still get a few of the top caliber students, but the number is not large in spite of attractive scholarships and active recruitment. A more basic change in the situation than the availability of scholarship help during training is going to be necessary to solve the problem.

This change, I think, will have to involve at least two conditions. First, there must be greater economic incentives; second, there must be an improvement in social attitudes toward academic careers. In the United States, the first will in time undoubtedly act toward bringing about the second.

The medical profession has, next to the public at large, the greatest stake in the solution of these problems. American medicine can coast for perhaps 10 years on its own momentum, but for the sake of the long-term future the American medical profession today should have at least as much interest in preventing deterioration as it had a half century ago, at the time of the Flexner report, in improving the status of medical education. The American Medical Association at that time led the crusade to eliminate inferiority and incompetence from medical education. It now has the opportunity to lead the forces working to maintain superior quality in American medical education. The American Medical Association won the battle in the first quarter of the century. The problem is undoubtedly more difficult today because it cannot be attacked through control of accreditation and licensure. Mediocrity cannot be prevented or abolished by law. It can only be eliminated by competition from superiority.

The positive weight of influence of the American Medical Association in favor of the use of some of the funds now devoted to the advancement of medical research in this country, or the provision of additional funds, for improvements in the quality of talent of persons entering academic careers in fundamental medical science would go far in accomplishing the objective. Such a position would be in line with the historic role of the Association in promoting excellence in American medicine and would strengthen the confidence of the public and the educational world in the sincerity of the Association in its claim to leadership in American medicine.

It is difficult to estimate the actual cost in teachers' salaries of medical education in the United States. This is partly because research and teaching functions are combined in varying ratios in the same persons. This is as it should be, but the research function should be recognized as such and research funds should properly carry their appropriate share of the total cost of academic staff salaries. This cannot be done unless medical research is supported on a more secure long-term basis than it is today. Universities cannot appoint permanent staff members on five-year grants. Institutions should, perhaps, have access to support that would allow them to appoint staff members at higher salaries to posts with life tenure through use, in part, of funds that are earmarked for research. On the other hand, more funds available to institutions for use interchangeably for either teaching or research might be preferable. There are undoubtedly many possible ways to solve the problem. The most important thing is the recognition that a serious problem exists. With that recognition will come, one may hope, a determination to solve it somehow. It would be an unbelievable stupidity if the richest country in the world were to handle its affairs so ineptly that it would one day soon approach the condition of the most underprivileged countries with regard to medical education. If it comes to such a pass here that "he who can, does. He who cannot, teaches." it will be a sorry day for American medicine. The dry rot of mediocrity can be the penalty of richness as well as poverty. It will, I predict, be our fate in medicine unless we move more vigorously and more intelligently than we have in the past decade.

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TEACHING OF ANESTHESIOLOGY IN MEDICAL SCHOOL

Gertie F. Marx, M.D.
and
Louis R. Orkin, M.D., New York

There is a continuing need for adequately trained anesthesiologists. Physicians and medical educators should recognize the importance of teaching anesthesiology to students and of including this specialty in the curriculum. The course here described provides for the introduction of certain graded work in each of the four years of the curriculum. It calls for careful integration with the work in other departments and for the active interest of the teaching staff. Although the teaching of anesthesiology as a specialty is primarily a postgraduate problem, this plan has been highly successful in focusing the student's attention on the fundamentals of anesthesia and resuscitation. It has also served to clarify the relationship of the patient as an individual with disease or diseases to the mental and physical trauma of an operation.

Anesthesiology is a youthful, vigorous specialty among medical disciplines. A national organization was founded in 1936 and incorporated under its present name, "American Society of Anesthesiologists," in 1945. The American Board of Anesthesiology was established as a major specialty board in 1942. Unbounded by traditions and unlimited by strict syllabus outlines, departments of anesthesiology have developed along many pathways.

This report concerns the philosophy and methodology employed in the instruction of students at the Albert Einstein College of Medicine, Yeshiva University. The teaching of anesthesiology is primarily a postgraduate problem, but a department functions in all four years of the curriculum. Two primary problems are undertaken here. The first centers about the belief that resuscitation is an important aspect of training, better taught to physicians by anesthesiologists than by lay groups. The second involves the relationship of the patient as an individual with disease or diseases to the mental and physical trauma of an operation. The solution of these necessitates teaching in all four years by an active, interested, enthusiastic staff.

First-Year and Second-Year Programs

During the first year, on completion of the anatomy program on the vertebral column and spinal cord, the department of anesthesiology offers a two-and-one-half-hour demonstration to the entire class. While the departmental chairman lectures on applied anatomy, members of the department demonstrate techniques on patients scheduled for operation. A conventional spinal block with the patient in the lateral recumbent position, a saddle block with the patient in the sitting position, a continuous epidural or caudal block, and a single-injection caudal block are started, each in a different patient. Cerebrospinal fluid is withdrawn. The collecting tubes, needles, and catheters are circulated among the students. While emphasis is placed on applied anatomy and not on technique, this demonstration is often the student's first encounter with actual pa-

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From the Bronx Municipal Hospital Center, Albert Einstein College of Medicine, Yeshiva University.

tients. It becomes an exciting and stimulating experience, leaving a lasting impression. The anatomists relate that the students study the complex anatomy of this region with renewed vigor and intent. The hours are available on invitation from the department of anatomy.

Four hourly didactic lectures and a three-hour demonstration are given in the second year during the course on pharmacology. The lectures cover primarily the theories of anesthetic action and the pharmacology of commonly employed general anesthetic drugs. A brief history of anesthesia is also included. The effects of inhalation agents and ancillary drugs are demonstrated on two patients before the entire class, with *continuous monitoring on oscilloscopes* of the electrocardiographic and electroencephalographic activities. Induction in the first patient is done with an intravenously given barbiturate and anesthesia is maintained with cyclopropane. An endoctracheal catheter is passed after the injection of succinylcholine, while fibrillatory and muscleblocking effects of paralyzing drugs are discussed. Thereafter, the action of trimethaphan (Arfonad) camphorsulfonate and phenylephrine (Neosynephrine) is shown. The second patient is subjected to anesthesia with a nitrous oxide–oxygen–ether sequence, and intubation is performed under deep ether maintenance. The effects of *d*-tubocurarine and edrophonium (Tensilon) chloride are demonstrated. The electrocardiographic findings characteristic of cyclopropane or ether anesthesia and the relationship of electroencephalographic activity to depth of anesthesia are seen on the oscilloscopes.

Third-Year Seminar

Time is allotted to the department for its own teaching program during the third year. Groups of five to six students are assigned to the service at the Bronx Municipal Hospital Center for a two-week period shared with the department of ophthalmology. The students attend anesthesiology sessions eight full mornings and two full afternoons. A program has been outlined, correlating 10 seminars with clinical activity in operating rooms, electroconvulsive therapy area, recovery rooms, and wards of the hospital. A copy of this outline is presented to the students with a suggested reading list. The first page, the "student's check sheet," is shown in table 1. All seminars are conducted by members of the attending staff. Emphasis is placed on resuscitation and the management of airway problems rather than on technical details of the conduction of anesthesia. The seminars are guided to elaborate the relationship of the patient, his diseases, and surgical requirements to the disciplines of anesthesiology.

The orientation seminar includes a brief history of the development of anesthesiology as a specialty and the role of the anesthesiologist in medical care. The former discusses the development of residency training, the American Society of Anesthesiologists, and the American Board of Anesthesiology. The latter encompasses the activities of the anesthesiologists in the operating theaters and in care of patients with pain problems, nerve blocks, and inhalation therapy in management of airway and respiratory problems, and as consultants throughout the hospital. The students are introduced to clinical problems by a tour of the operating room suites and a demonstration of equipment, both research and clinical. An anesthesia machine is dissected in detail, and fire and explosion hazards are explained.

The second seminar, an afternoon session, deals with the interpretation and importance of anesthesia records, the value and procedure of the preoperative and postoperative visits, and preoperative care and medication. The students are assigned patients for the next morning and proceed to preoperative rounds on these patients with a senior resident. At 4 p.m. they attend and participate in the department's weekly "case report conference."

TABLE 1.—*Anesthesiology Student's Check Sheet at Bronx Municipal Hospital Center**

Name..From...............To...............

Seminars	Practical
Orientation	Demonstration of anesthesia equipment
Charting, preoperative and postoperative visit	Preoperative visit
Airway problems and resuscitation, coma and cardiac arrest	Resuscitation Model Patient
Inhalation anesthesia	Demonstration of
Regional anesthesia	Inhalation anesthesia
Physics and oxygen therapy	Intravenous anesthesia
Postoperative care, recovery room	Rectal anesthesia Spinal anesthesia
Discussion of classic case reports, 1	Electroconvulsive therapy clinic
Discussion of classic case reports, 2	Postoperative visit
Discussion of students' case reports	

*Each student is required to submit summary of case—preoperative considerations, anesthetic management, and postoperative course—at last seminar. Recommended reading: Dripps and others[1]; Schwartz, H., and others: Manual of Anesthesiology, Springfield, Ill., Charles C Thomas, Publisher, 1957; Cullen, S. C.: Anesthesia in General Practice, ed. 4, Chicago, Year Book Publishers, Inc., 1954.

The next morning, the students observe the course of anesthesia and operation in the patients seen the preceding afternoon. They start the intravenous infusion, monitor pulse and blood pressure, and maintain the anesthesia record. Once the situation is stabilized, they are allowed to get the "feel of the bag" and conduct the anesthesia with the resident. The seminar consists of a lecture on inhalation anesthesia.

The following morning is devoted entirely to the problems of airway maintenance. A lecture and exhibition of various methods of resuscitation on a life-size model of the upper respiratory tract is followed by a demonstration on an anesthetized patient. The students participate in the insertion of oropharyngeal and nasopharyngeal airways and the administration of oxygen by mask and bag. Laryngoscopy is demonstrated in a patient and on the model by an instructor. The students practice on the latter (fig. 1). Resuscitation apparatus is shown, but special emphasis is placed on mouth-to-mouth and mouth-to-airway breathing (fig. 2). The management of coma, convulsion, drug poisoning, drowning, "cardiac arrest," and other catastrophic emergencies is also discussed.

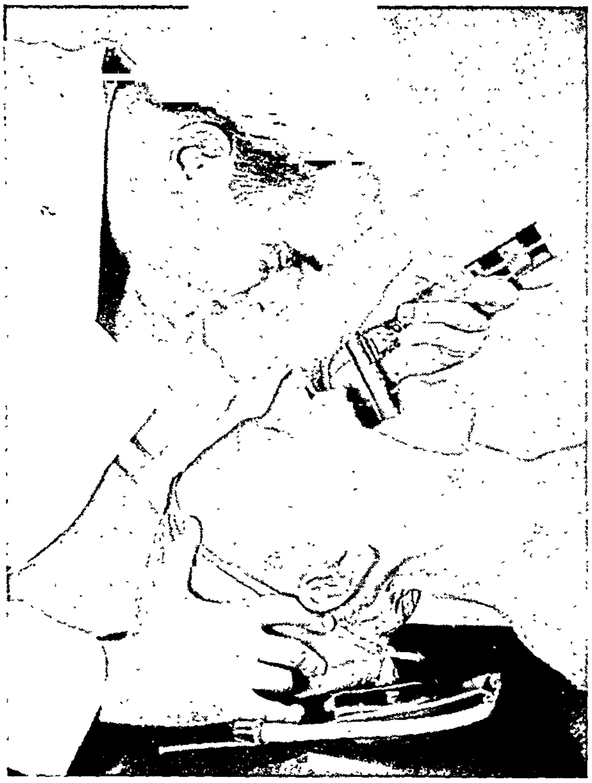

Fig. 1.—Laryngoscopy as practiced on life-size model of upper respiratory tract.

The final session of the first week is spent in the electroconvulsive therapy clinic. Under the guidance of a senior member of the staff, the students use this opportunity to administer intravenous anesthetic agents and muscle relaxants and to maintain an unconscious, paralyzed patient. Maintenance with and without an airway is practiced. Ventilation is performed by the students in the manner previously learned, including mask and bag techniques. A seminar on regional anesthesia follows. The seminars on inhalation and regional anesthesia are correlations of the operating room observations and activities to the physiological and pharmacological characteristics of the techniques and agents. They include reviews of anatomy, physiology, pharmacology, and pathophysiology.

Mornings of the second week are spent in elaboration and extension of the operating room activities of the first week. The students are given additional tasks and allowed to administer anesthesia to relatively healthy patients requiring minor surgical procedures. They are never without supervision. During this week the students spend an additional session in the electroconvulsive therapy clinic. They are present during administration of nerve block anesthesia and are in attendance during cardiac surgery.

The first seminar of this week includes the physics of medicinal gases and of ventilation, carbon dioxide retention, vaporization of fluids, and the application to oxygen therapy. The afternoon seminar deals with postoperative care, the role of a recovery room, and of postoperative visits. On this afternoon, the students again attend the case report conference. The eighth and ninth seminars are devoted to discussions of cases selected from departmental files. The cases chosen present problems related to the broad sphere of medicine, such as blood pressure fluctuations during operation and anesthesia, postoperative hypotension, hypoglycemia in a surgical patient with recent hepatitis, or postoperative pulmonary edema from overloading with intravenously given fluids.

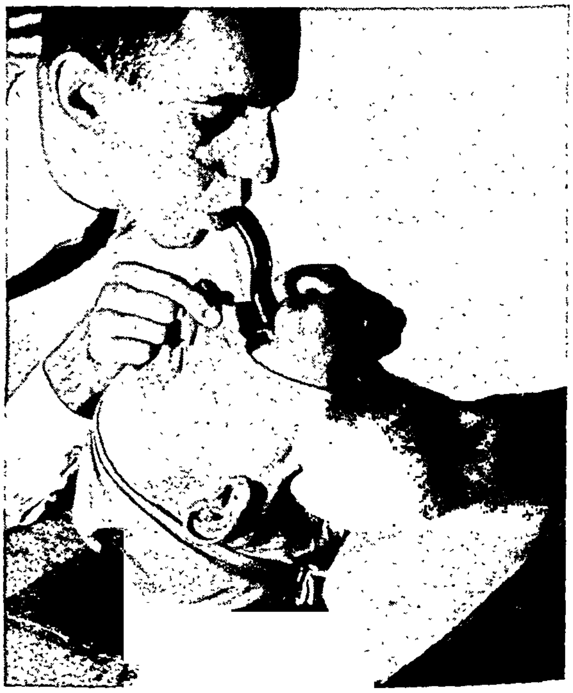

Fig. 2.—Mouth-to-airway breathing as practiced on life-size model of upper respiratory tract.

In the final seminar, each student submits a copy of a written report on the management of the patient he saw through preoperative visit, anesthesia, and postoperative period. An outline explained and given to the students during the second seminar is used as a guide (table 2). The reports form the material for discussion.

Final Lectures and Comment

During the fourth year only two formal lectures are offered to the whole class by the department. These are utilized to elaborate and renew concepts of resuscitation and the treatment of coma. For those students desiring to learn techniques of anesthesia, a two-month elective is offered during the year. Six per cent of the class has taken advantage of this opportunity. Attendance is limited to two students per period. The students electing this service are appointed as substitute interns. They share the activities of the residents with the exception that they may not administer anesthesia without supervision. The department of obstetrics invites one-third of the senior class at a time to a lecture on infant resuscitation.

The outlined curriculum has proved highly successful. Many students have expressed their enthusiasm for the third-year program to their student counselors. Within a framework of 40 hours during the third year, the objectives outlined can be accomplished but only at the expense of personal continuous effort by senior members of the department. Only a few American medical schools have recognized the importance of teaching anesthesiology to students and have prepared a program including this specialty in their curriculum. Dripps and associates[1] recommend clinics during the preclinical years on artificial ventilation, on applied anatomy of regional anesthesia, and on applied pharmacology of drugs used in anesthesia. In the clinical years, seminars, correlation clinics, and experience are offered. Greene[2] writes that those teaching anesthesiology "should be primarily teachers of medicine and secondarily teachers of anesthesia." We cannot but endorse the wide approach to the teaching of anesthesiology rather than the narrow technical aspect. On proper presentation of the scope of the specialty to the undergraduate, there will be no dearth of interns preparing for further training and, some day, no lack of adequately trained anesthesiologists to care for the American public. It needs only effort and interest to teach the value of this subject to physicians and medical educators.

TABLE 2.—*Outline of Anesthesia Report as Used by Students at Bronx Municipal Hospital Center*

Student's Name..Date..................

Patient's Name..Age........Ward.........

History No............................Anesthesia No..............................

A. Pertinent history and physical findings
B. Laboratory data
C. *Procedure contemplated*
D. Choice of anesthesia
  1. Drugs and techniques
  2. Problems relative to
    a. physiological-pathological changes
    b. particular needs at operation
E. Short description of anesthetic management used
  1. Agents
  2. Techniques
  3. Supportive therapy
F. Postoperative follow-up study
  1. Complications, causes
  2. Therapy

Eastchester Road and Morris Park Avenue (61) (Dr. Marx).

References

1. Dripps, R. D.; Eckenhoff, J. E.; and Vandam, L. D.: Introduction to Anesthesia: Principles of Safe Practice, Philadelphia, W. B. Saunders Company, 1957, pp. 250-252.

2. Greene, N. M.: *Role of and Responsibilities of Department of Anesthesia in University Hospital*, J. M. Educ. **31**:684-690 (Oct., pt. 1) 1956.

EFFECT OF ALCOHOL ON THE ELECTROENCEPHALOGRAM.—The noteworthy effect of alcohol on the EEG consists of the production of sequences of 4-8 cycle waves, with persistence of alpha rhythm in the intervals. The slowing in a given individual is roughly proportional to the concentration of alcohol in the blood, and usually becomes manifest at about the concentration at which obvious signs of intoxication, such as trouble with balance, appear. The same variation in tolerance to alcohol is seen in the effect on the EEG as in other evidence of intoxication. In the small group investigated a tendency was apparent for individuals with more experience with alcohol to show a high tolerance both clinically and electroencephalographically. The EEG change produced by alcohol cannot be produced by any psychological mechanism, either at a conscious or subconscious level. Neither can it be produced as a consequence of any vasomotor or other autonomic change secondary to the emotional state. The reasonable assumption is, therefore, that it is a reflection of the same disordered neuronal activity that is manifested in the more readily assessed attributes of drunkeness.—H. W. Newman, M.D., The Effect of Alcohol on the Electroencephalogram, *Stanford Medical Bulletin*, May, 1959.

VIRAL DISEASE OF THE CENTRAL NERVOUS SYSTEM

INFLUENCE OF POLIOMYELITIS VACCINATION ON ETIOLOGY

Edwin H. Lennette, M.D., Ph.D., Robert L. Magoffin, M.D., M.P.H., Nathalie J. Schmidt, Ph.D.
and
Arthur C. Hollister Jr., M.D., M.P.H., Berkeley, Calif.

Viral studies were made of 1,407 patients with clinical manifestations of infectious disease involving the central nervous system. Both virus isolation and serologic methods were used. The results showed apparent differences in the etiology of clinical poliomyelitis and aseptic meningitis which correlated with the degree of prior immunization with inactivated poliovirus vaccine. Poliovirus was identified less often, and other viruses more often, among patients with both paralytic and nonparalytic illness who had received the vaccine. The findings also indicated that "nonpolio" enteroviruses have protein pathogenic capabilities enabling them to give rise to a broad spectrum of syndromes embracing the clinical picture of aseptic meningitis, mild to moderate paralytic poliomyelitis, and meningoencephalitis.

A number of investigators have reported the recovery of Coxsackie group B viruses,[1] Coxsackie group A viruses,[2] and several types of ECHO viruses [3] from patients given a clinical diagnosis of nonparalytic poliomyelitis or aseptic meningitis. Certain serotypes of Coxsackie and ECHO viruses have also been etiologically incriminated [4] in some illnesses resembling paralytic poliomyelitis. In a few instances, encephalitic manifestations have also been associated with infection with some serotypes of Coxsackie B virus.

Since these enteroviruses have been found also in fecal samples from normal, non-ill population groups, their etiological significance when found in association with illness, particularly sporadic cases, is often equivocal. That certain types of Coxsackie and ECHO viruses are important causative agents of the aseptic meningitis syndrome is now well established,[5] but further observations are needed to assess their etiological importance in encephalitic and paralytic illnesses.

The advent of killed-virus vaccine has heightened the need to determine how often other viruses may be responsible for illnesses clinically resembling poliomyelitis. Thus, Davis and Melnick [1b] found that poliovirus infection was appreciably less often confirmed in both paralytic and nonparalytic cases of poliomyelitis in patients who had received the vaccine as compared with those who had not.

The purpose of this report is to present a summary of laboratory findings from a three-year study of cases of poliomyelitis, aseptic meningitis, and encephalitis in California, with particular reference to apparent differences in the etiology of illness in vaccinated and nonvaccinated patients.

Study Plan

The laboratory studies described herein were conducted in conjunction with the poliomyelitis surveillance program initiated by the California State Department of Public Health in June, 1955. Close cooperation was maintained with the epidemiology and laboratory branches of the Communicable Disease Center of the United States Public Health Service, Atlanta, Ga. Individual case histories, including clinical and epidemiologic data, and specimens for laboratory study were obtained through the cooperation of local health officers.

Initially, in 1955, only cases clinically diagnosed as poliomyelitis, paralytic and nonparalytic, received laboratory study. In 1956 and 1957, the study was extended to cover a broader spectrum of acute infectious diseases involving the central nervous system (C. N. S.), including clinical designations such as aseptic meningitis, encephalitis, and "viral C. N. S. disease," in addition to unqualified diagnoses of poliomyelitis.

Specimens for laboratory study were requested as follows: three or four stools, collected at one-to-three day intervals during the acute phase of illness, and three blood specimens, taken, respectively, when the patient was first seen, 14 days after onset, and four to six weeks after onset. An effort was made to obtain specimens on all patients who had received one or more doses of vaccine and on selected control groups of nonvaccinated patients. In 1955, specimens were requested from all nonvaccinated patients aged 6 to 9 years, to correspond with the age group in which the vaccination effort was concentrated at that time. In 1956 and subsequently, specimen collection from nonvaccinated patients was broadened to include patients of all ages in several selected counties. In this way the

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From the Viral and Rickettsial Disease Laboratory and the Bureau of Acute Communicable Diseases, California State Department of Public Health.

number of nonvaccinated patients subjected to laboratory study approximately balanced the number of vaccinated patients.

Isolation and Identification of Viruses

Stool suspensions were inoculated into monkey-kidney cell cultures for the detection of poliovirus or other cytopathogenic agents. Specimens from about 500 stools, from 250 patients, were also inoculated into suckling mice. All virus isolates were typed either in monkey-kidney cell cultures or colorimetrically in cultures of the FL line of human amnion cells,[5A] with use of monkey-immune serum for each of the three types of poliovirus, Coxsackie virus types B1-B5, and type A9. Isolates obtained in suckling mice were identified by neutralization tests with specific antiserums in suckling mice. Isolates not identified by these procedures are still in the process of being typed against available type-specific serums to the ECHO viruses. Results of the typing to date indicate that ECHO virus types 4, 6, and 9 are represented in this group, but the majority of strains have not been specifically identified. Pending specific identification, these isolates are referred to in this report as "unidentified ECHO viruses."

Serologic Tests

Serologic procedures included complement-fixation (CF) tests for poliomyelitis types 1, 2, and 3[6]; mumps; western equine encephalomyelitis; epidemic (St. Louis type) encephalitis; and herpes simplex. Initially, serologic tests other than for poliomyelitis were conducted somewhat selectively, and no further tests were done when a positive result was encountered. Later, the complete series of CF tests was done uniformly on each patient. During the first two years of the study a colorimetric neutralization test for poliomyelitis was also included routinely, but, because of the small additional diagnostic returns from this test, it was used selectively during the last year.

Results

Isolation of Enteric Viruses.—From June, 1955, through December, 1957, fecal specimens were examined from 1,407 patients suspected to have an infectious disease involving the central nervous system. The clinical diagnoses could be grouped, as shown in table 1, into one of six categories: paralytic poliomyelitis, 497 cases; nonparalytic poliomyelitis, 593 cases; aseptic meningitis, 120 cases; encephalitis, 124 cases; other diagnoses of C. N. S. disease, 39 cases; and 34 cases of miscellaneous febrile illnesses in which no definite signs of C. N. S. involvement were observed. Grouping was based on the clinical diagnosis as recorded at the conclusion of the acute phase of illness but prior to knowledge of the results of viral studies. In most instances this was the diagnosis given at hospital discharge.

The category aseptic meningitis includes closely similar diagnostic terms such as viral meningitis, nonpurulent meningitis, and benign lymphocytic meningitis. Unqualified diagnoses of nonparalytic poliomyelitis were treated as a separate category. Diagnoses of paralytic poliomyelitis were, in most cases, unqualified. Although in many instances clinical histories indicated that there was only mild impairment of muscle strength, some degree of demonstrable paresis persisting after the acute febrile phase of illness or at the time of hospital discharge was recorded for all cases classified as paralytic poliomyelitis.

The term "encephalitis" includes clinical diagnoses of acute infectious encephalitis, meningoencephalitis, or encephalomyelitis. The category of "other C. N. S. illness" includes cases in which an initial clinical impression of a possible viral C. N. S. disease was discarded on further observation, e. g., purulent meningitis, Guillain-Barré syndrome, Bell's palsy, and cerebral vascular lesion. The term "no C. N. S." refers to patients hospitalized with acute febrile illnesses in which the initial suspicion of C. N. S. involvement was not confirmed, e. g., uncomplicated measles, mumps, influenza-like illnesses, and acute gastroenteritis.

Table 1.—*Recovery of Enteroviruses from Patients Hospitalized with Suspected Central Nervous System Disease, California, 1955 to 1957*

Clinical Diagnosis	Total Cases Studied, No.	Virus Isolated, %				No Virus Isolated, %
		Total	Poliovirus	Coxsackie	ECHO (Unidentified)	
Total	1,407	44	24	14	6	56
Paralytic poliomyelitis	497	62	54	5	3	38
Nonparalytic poliomyelitis	593	39	9	21	9	61
Aseptic meningitis	120	45	6	29	10	55
Encephalitis	124	22	2	17	3	78
Other C. N. S. disease	39	13	3	10	0	87
No signs of C. N. S. disease	34	3	3	0	0	97
Cases, no.		624	331	207	86	783

Of the 1,407 patients studied over a three-year period in these clinical categories, 624, or 44%, yielded an enterovirus. Polioviruses were isolated from 331, or 24%, and unidentified ECHO viruses were isolated from 86, or 6%, of the total patients. In 14 instances two different viruses were recovered from the same person. To avoid confusion of numbers in table 1, only one of the isolates from these patients was counted; these patients are considered again later.

Of the 497 patients clinically classified as having paralytic poliomyelitis, poliovirus was recovered from 54%. This low rate of laboratory confirmation of presumed poliovirus infection represents a further decline from rates of about 75%[7] and 60%[8] reported previously from this laboratory and is in contrast with earlier reports by others who recovered poliovirus from about 90% of paralyzed patients.[9] The discrepancy between these various estimates of the effectiveness of the laboratory diagnosis of poliomyelitis by recovery of the virus from stools is more readily understandable in the light of the variations in virus recovery described below in relation to the age and vaccination status of the patients studied.

Poliovirus was recovered from only 9% of the patients given a clinical diagnosis of nonparalytic poliomyelitis and 6% of those given a diagnosis of aseptic meningitis. Two patients with encephalitis (2%), one patient considered to have Bell's palsy, and one patient with an influenza-like syndrome yielded poliovirus. Coxsackie viruses, including group B, types 2, 3, 4, and 5, and group A, type 9, were recovered from 5% of the patients with clinically diagnosed paralytic poliomyelitis, 21% of those with nonparalytic poliomyelitis, 29% of those with aseptic meningitis, 17% of those with encephalitis, and 10% of those with other diagnoses of C. N. S. disease. ECHO (unidentified) viruses were recovered from about 10% of the patients with nonparalytic poliomyelitis and aseptic meningitis, 3% of those with paralytic poliomyelitis, and 3% of those with encephalitis. It is apparent that the recovery of enteroviruses was not notably different between cases clinically diagnosed as nonparalytic poliomyelitis and those diagnosed as aseptic meningitis.

Serotypes of Polioviruses and Coxsackie Viruses.—The specific serotypes of the polioviruses and Coxsackie viruses recovered from patients in each clinical category are shown in table 2. In the 331 patients yielding a poliovirus, type 1 virus was found in 266, type 3 in 57, and type 2 in only 8. There was no apparent difference in the distribution of poliovirus types recovered in paralytic and nonparalytic patients.

The predominant Coxsackie virus types were B5, recovered from 79 patients, and B4, recovered from 74 patients. Together, these accounted for nearly 75% of the 207 patients yielding a Coxsackie virus. Other types identified were B2, B3, A4, and A9; type B1 was not encountered. A single isolation of type A4 was made in suckling mice. Since only monkey-kidney cell cultures were used uniformly for virus isolation, the data concerning the occurrence of Coxsackie group A viruses are incomplete other than for type A9, which is readily recovered in this cell system.[7] Each type of Coxsackie virus tended to conform to the same pattern of disease association, being associated most frequently with cases of aseptic meningitis or nonparalytic poliomyelitis, somewhat less often with encephalitis, and infrequently with paralytic poliomyelitis.

Annual Differences in Distribution of Coxsackie Virus Types.—Considerable differences were noted in the occurrence of particular types of Coxsackie virus from one year to another. For example, in 1955, Coxsackie viruses A9 and B2 were the most common types. In 1956, type B5 accounted for about two-thirds of the Coxsackie viruses isolated. In 1957, isolations of type B5 declined and B4 was the predominant type. Although varying in relative frequency, all of the types shown in table 2 (except type A4) were encountered each year.

Age and Vaccination Status.—Differences in the recovery of enteroviruses from patients in each clinical category according to the patient's age and poliomyelitis vaccination status are illustrated in the figure. Patients who had received the vaccine were divided into two groups: those who had received a single dose and those who had received two or more doses. Patients given a second dose less than 15 days prior to onset of illness were included with the single-dose group. The small number of vaccinated patients over the age of 15

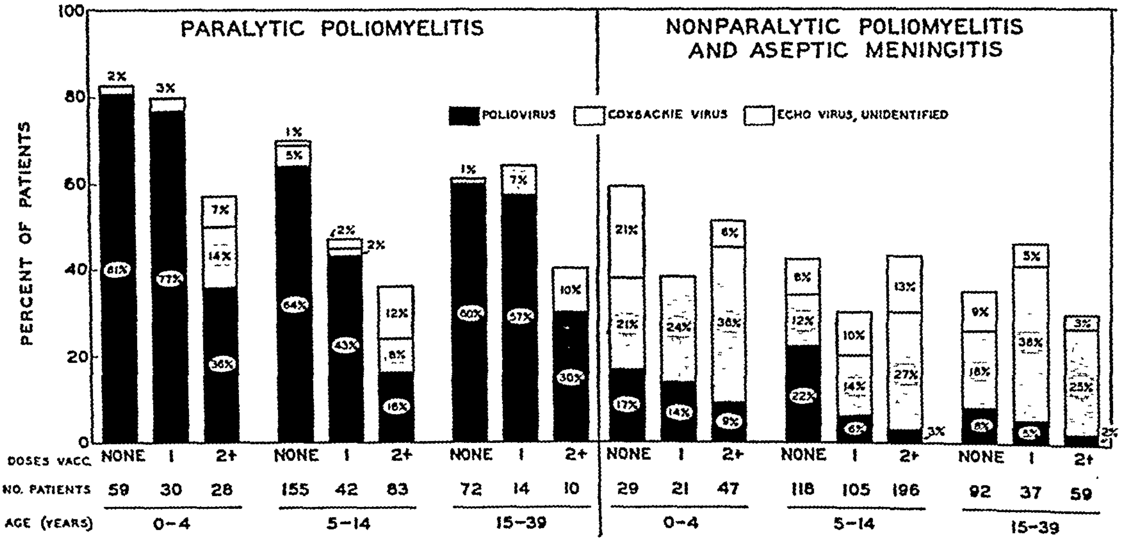
TABLE 2.—*Distribution, by Clinical Diagnosis and Immunotype, of Enteroviruses Recovered from Patients Hospitalized with Suspected Central Nervous System Disease, California, 1955 to 1957*

Clinical Diagnosis	Patients from Whom Virus Was Isolated, No.	Poliovirus, Type				Coxsackie Virus, Type							ECHO (Unidentified)
		Total	1	2	3	Total	A4	A9	B2	B3	B4	B5	
By number													
Paralytic poliomyelitis	307	267	213	4	50	24	..	3	6	1	7	7	16
Nonparalytic poliomyelitis	230	53	43	4	6	123	..	13	12	7	46	45	54
Aseptic meningitis	54	7	7	..	..	35	1	3	1	..	14	16	12
Encephalitis	27	2	1	..	1	21	..	..	2	3	7	9	4
Other	6	2	2	..	..	4	..	..	1	1	..	2	..
Total	624	331	266	8	57	207	1	19	22	12	74	79	86
By percent													
Paralytic poliomyelitis	100	87	69	1	16	8	0	1	2	+	2	2	5
Nonparalytic poliomyelitis	100	23	19	2	3	54	0	6	5	3	20	20	23
Aseptic meningitis	100	13	13	0	0	65	2	6	2	0	26	30	22
Encephalitis	100	7	4	0	4	78	0	0	7	11	26	33	15
Other	100	33	33	0	0	67	0	0	17	17	0	33	0
Total	100	53	43	1	9	33	+*	3	4	2	12	13	14

*+=<0.5%.

years did not permit a finer breakdown beyond this age. Only 11 of the 1,407 patients in the entire study were aged 40 or over.

Differences in the recovery of poliovirus with respect to age and immunization status were most striking among patients classified as having paralytic poliomyelitis. In this category, in the absence of vaccination, poliovirus was recovered from 81% of the children under 5 years of age, 64% of those 5 to 14, and 60% of those 15 to 39. Thus, apart from the influence of vaccination, poliovirus infection was appreciably more often confirmed in small children with paralytic illness than in older children and adults. In each age group, the recovery of poliovirus was slightly lower from the patients vaccinated with a single dose and markedly lower from those who had received two or more doses, dropping to 36% of cases in the 0-to-4-year age group, 16% in the 5-to-14-year age group, and 30% in the 15-to-39-year age group. There were only 21 patients (not shown separately in figure 1) classified as having paralytic poliomyelitis who had received three or more doses of vaccine; these were mostly in the 5-to-14-year age group. Only one yielded poliovirus.



Recovery of enteroviruses from patients with poliomyelitis or aseptic meningitis, according to age group and doses of vaccine —California, 1955-1957.

The lower recovery of polioviruses from vaccinated patients with paralytic illness was attended by a higher recovery of Coxsackie and unidentified ECHO viruses. This was particularly evident in the 0-to-4-year and 5-to-14-year age groups, in which substantial numbers of vaccinated patients were available for study. In these two age groups, "nonpolio" enteroviruses were recovered from about 20% of the paralytic patients who had received two or more doses of vaccine. Nevertheless, the percentage of patients whose stools did not yield any virus was appreciably higher among the vaccinated than among the nonvaccinated persons. Together, the combined influence of age and vaccination produced a remarkable range of variation in the laboratory confirmation of poliomyelitis among patients with paralytic illness, from recovery of the virus in 80% of nonvaccinated patients under the age of 5 years to an inability to recover the virus in approximately 70 to 85% in older patients who had received two or more inoculations of vaccine.

In patients with nonparalytic poliomyelitis and aseptic meningitis, in the absence of vaccination, poliovirus was isolated in from 17 to 22% of those under the age of 15 years and 8% of those aged 15 to 39. As in paralytic disease, recovery of poliovirus was consistently lower among immunized patients, falling to 9% among children under 5 years of age and 2 to 3% among older patients who had received two or more doses of vaccine. Coxsackie viruses, present in 12 to 25% of the nonvaccinated persons, were more frequently recovered in the vaccinated patients, exceeding poliovirus isolations by 4 to 10 times. Unidentified viruses were encountered in 9 to 21% of nonvaccinated and in 3 to 13% of vaccinated patients, but no definite pattern of occurrence in relation to vaccination status was evident among patients with nonparalytic illness.

In 121 cases of clinical encephalitis only two isolations of poliovirus were made, both in nonvaccinated patients under 15 years of age. Coxsackie viruses were recovered in 18 to 22% of the patients under age 15 and were about equally distributed in vaccinated (18% in those given one dose and 22% in those given two or more doses) and nonvaccinated patients (22%); unidentified ECHO viruses were recovered from one nonvaccinated patient (3%) and 3 vaccinated (2 or more doses) patients (8%) under age 15. No virus was recovered from the 13 vaccinated patients over age 15.

Among 73 patients with other illnesses, two isolations of poliovirus and four isolations of Coxsackie virus were made. All but one of these patients had manifestations of a C. N. S. disease not clinically classified as poliomyelitis, aseptic meningitis, or encephalitis. The virus isolations in this group of cases were too few to warrant further analysis.

The markedly less frequent recovery of poliovirus from vaccinated patients given a clinical diagnosis of poliomyelitis, paralytic or nonparalytic, than from nonvaccinated patients, may be interpreted in either of two ways: (1) that the administration of the vaccine reduced excretion of virus or in some other way influenced the recovery of poliovirus from patients whose illness was actually due to poliovirus infection or (2) that the illnesses observed in vaccinated patients were, in fact, less often due to poliovirus infection and more often due to other causes. The latter interpretation is supported by the more frequent recovery of other agents from vaccinated patients and by the results of serologic tests as described below.

Serologic Evidence of Etiology.—In our experience patients yielding poliovirus in the feces have only occasionally failed to develop complement-fixing antibodies and have virtually invariably had demonstrable neutralizing antibodies in convalescent-phase serum samples.[10] In the present study, among patients yielding poliovirus, complement-fixing antibody was present at a titer of 1:4 or greater in over 90% of the serums of convalescent patients; a fourfold or greater rise in complement-fixing antibody titer during the course of illness was demonstrated in about 55% of the patients.

Complement-fixation tests for poliomyelitis, mumps, western equine encephalomyelitis, St. Louis type encephalitis, and herpes simplex were performed on the serums of a group of 663 patients whose stools did not yield an enterovirus. High antibody levels were recorded in the absence of a fourfold rise in antibody titers; high titers were defined as levels of 1:32 or higher against poliovirus or mumps virus antigens and levels of 1:16 or higher against antigens of western equine encephalomyelitis or antigens of St. Louis type encephalitis. High stationary titers (1:64 or greater) to herpes simplex were commonly encountered in patients with antibody rises to other agents; elevated antibody titers to more than one of the other viruses were rarely present. Hence, with respect to herpes simplex virus, only titer rises were considered. Antibody titers below these specified levels to any one of these agents were considered as inconclusive; such antibody levels were often present to more than one agent. The term negative referred to absence of complement-fixing antibody in the lowest dilution of serum tested: 1:4 in the poliomyelitis CF test and 1:8 for all others.

Serologic evidence of poliovirus infection, either a fourfold rise in complement-fixing antibody titer (6%) or an elevated titer (2%) was elicited in only 8% (12 patients) of the 155 patients with clinical paralytic disease whose stools failed to yield a virus. A fourfold titer rise in antibody to the mumps virus was found in 6% of the patients and rises in antibody to St. Louis type encephalitis and herpes simplex viruses in 1% of the cases. Nearly one-half of the paralytic patients had only low stationary titers to one or more agents, and in one-third of the cases all the CF test results were negative. If the results of the poliomyelitis CF test are considered separately, one-third of the patients had "inconclusive" titers of antibody and nearly one-half had no demonstrable antibody. Although infrequent in either group, rises in poliomyelitis antibody titer or elevated titers were found less than one-half as often among vaccinated as among nonvaccinated patients. Serologic evidence of other virus infections was predominantly in the vaccinated group.

Among the 305 patients given a diagnosis of nonparalytic poliomyelitis and who failed to yield an enterovirus, rises in antibody titer were found in 2% and high titers in an additional 2%. No rises in poliomyelitis antibody titer were encountered among patients with aseptic meningitis or encephalitis, and high titers were infrequently present. Inconclusive levels of poliomyelitis antibody, however, were frequently encountered in all clinical categories, a strong indication that such titers were, in general, a reflection of past infection and unrelated to the current illness.

Poliovirus neutralizing antibody determinations were also made on the serums from 340 of the patients whose CF test results were inconclusive or negative. Poliomyelitis infection was evidenced by significant rises in antibody in eight of these patients, approximately 2% of those tested, including one patient with paralytic illness, six with nonparalytic illness, and one with an influenza-like illness. The results of both serologic tests thus strengthen the conclusion that relatively few poliovirus infections had been missed by stool cultures.

Evidence of mumps virus infection was the most frequent positive serologic finding among patients with nonparalytic poliomyelitis, aseptic meningitis, or encephalitis; significant titer rises were seen in about 10% of the cases in each of these clinical categories and elevated titers in an additional 2 to 10% of the cases. Significant titer rises to western equine encephalomyelitis or St. Louis type encephalitis viruses were found in an occasional patient thought to have nonparalytic poliomyelitis and in 5% of the patients with encephalitis. Titer rises indicative of primary infection with herpes simplex virus were present in three cases (1%) of nonparalytic poliomyelitis and two cases of encephalitis. In each clinical category, the percentage of patients having positive serologic findings was greatly exceeded by the percentage of those in whom all tests were inconclusive or negative.

In summary, the serologic findings added less than 10% to the number of illnesses already confirmed as poliomyelitis by isolation of the virus. Serologic evidence of poliovirus infection in the absence of virus excretion was less frequently elicited in vaccinated patients. Serologic evidence of mumps, St. Louis type encephalitis, western equine encephalomyelitis, or herpes simplex virus infection was encountered primarily in cases of aseptic meningitis and encephalitis, occasionally in paralytic illnesses, particularly in the vaccinated patients.

Concurrent Infection with More Than One Agent.—The battery of laboratory tests used provided an opportunity to assess the frequency of concurrent infection with two or more viruses. The inoculation of stools from about 250 patients into suckling mice offered a selective medium for the emergence of those Coxsackie viruses which do not multiply in tissue cultures, or those which might have been overgrown in such cultures by polioviruses or ECHO viruses if more than one agent were present. Tissue cultures behaving atypically with respect to cytopathogenesis were treated with selected antiserums to detect possible mixtures of two agents. Serologic tests provided opportunity to detect the occurrence of poliovirus infection in patients excreting Coxsackie or ECHO viruses and of mumps virus infection in patients excreting poliomyelitis, Coxsackie, or ECHO viruses.

In 14 patients, two different viruses were recovered from the feces, usually from separate specimens collected on different days. These dual isolations occurred in 1% of 331 patients from whom a poliovirus was isolated, 5% of 216 patients from whom a Coxsackie virus was isolated, and 11% of 97 patients from whom an unidentified ECHO virus was isolated. Unidentified ECHO viruses isolated from patients who also yielded a poliovirus or Coxsackie virus accounted for 11 of the 14 instances in which two viruses were recovered. These unidentified agents were detected more frequently with a Coxsackie virus (nine patients) than with a poliovirus (two patients). Coxsackie virus (B4) and poliovirus (type 1) were isolated from the same person in only one instance; one patient yielded poliovirus types 1 and 2, and another yielded Coxsackie viruses B4 and B5.

Among 185 patients shedding poliovirus and from whom paired serums were tested for complement-fixing antibody to mumps, western equine encephalomyelitis, St. Louis type encephalitis, and herpes simplex viruses, 2 persons (about 1%) showed significant titer rises to mumps; no other titer rises were found. Of 123 patients yielding Coxsackie virus, and having a complete serologic study, a significant rise in poliomyelitis complement-fixing antibody was demonstrated in 3 and a rise in western equine encephalomyelitis antibody in 1, a total of 3% having serologic evidence of a dual infection. Among 45 patients yielding unidentified viruses whose serums were completely tested, a significant rise in poliomyelitis complement-fixing antibody was found in 6 and a rise in mumps antibody in 1, making a total of 16% of this group having evidence of a dual infection. The three cases mentioned above in which a significant rise in mumps antibody was associated with the recovery of an enterovirus (two associated with poliovirus isolations and one with an unidentified enteric virus) were the only instances of multiple infections demonstrated among 53 patients (6%) having a significant rise in mumps antibody.

When the virus isolation and serologic data are combined and extrapolated, they give evidence that, among patients excreting a poliovirus, another virus infection was present in about 2%; of those yielding

TABLE 3.—*Summary of Laboratory Findings in Patients with Acute Central Nervous System Disease, California 1955 to 1957*

		% of Group										
			Virus Isolated, or Serologic Evidence of Infection						No Virus Isolated			
Clinical Diagnosis and Vaccination Status	Patients, No.	Total	Polio-myelitis	Cox-sackie	ECHO Unidentified	Mumps	Herpes, Simplex	Mixed Infections	Total	Serologic Test Results Inconclusive	Serologic Test Results Negative	Serologic Tests Not Done
Paralytic poliomyelitis	497	100	57	5	3	3	1	1	30	14	10	7
Nonvaccinated	290	100	70	3	1	0	+	1	25	9	7	10
1 dose	86	100	62	3	1	8	0	0	28	19	7	1
2 or more doses	121	100	21	8	9	5	3	3	48	23	21	4
Nonparalytic poliomyelitis	593	100	11	20	8	6	1	2	52	24	18	10
Nonvaccinated	206	100	17	12	9	5	+	2	55	23	15	17
1 dose	150	100	11	21	6	10	1	1	50	25	19	7
2 or more doses	237	100	6	26	9	5	3	2	49	24	19	6
Aseptic meningitis	120	100	4	28	9	8	2	3	16	24	18	3
Nonvaccinated	38	100	8	29	5	0	0	5	53	29	24	0
Vaccinated	82	100	2	28	11	11	2	2	44	22	16	5
Encephalitis	124	100	5	15	2	12	7	3	56	24	19	12
Nonvaccinated	62	100	6	15	0	13	3	5	58	29	18	11
Vaccinated	62	100	3	15	5	11	11	2	53	19	21	13

a Coxsackie virus, approximately 8% also had evidence of another virus infection. Among patients yielding an unidentified enterovirus, the data are less complete but suggest that about 25% were also infected with another virus.

These findings serve to emphasize the difficulties and chances for error in attempting to ascribe etiological significance to an enterovirus recovered from any particular patient; on the other hand, it is evident from the data as a whole that laboratory evidence of more than one possible etiological agent was infrequently found.

Summary of Laboratory Evidence of Etiology.—The results of virus isolation attempts and serologic examinations are collated and summarized according to the patient's clinical diagnosis in table 3.

The marked decline in confirmed poliovirus infections, from 70% in nonvaccinated to 24% in vaccinated patients with paralytic illness, is again evident. Coxsackie, mumps, herpes simplex, St. Louis type encephalitis, and unidentified ECHO viruses were each associated with some cases of paralytic disease in which evidence of poliovirus infection was lacking. The frequency of these infections, 1 to 5% of the total cases studied, appears to be well within the range of coincidental occurrence; however, a fairly consistent increase in the occurrence of these viruses is discernible among vaccinated patients. Altogether, nonpoliovirus infections were found in 25% of the vaccinated (two-dose) paralytic patients in the absence of any other positive findings. Paralytic illnesses in which poliovirus could not be recovered and in which serologic tests were negative or inconclusive were also much more frequently encountered among the vaccinated patients, comprising over 40% of the two-dose group.

In the other clinical categories of illness, Coxsackie viruses were generally associated more frequently than any other virus with illnesses diagnosed as nonparalytic poliomyelitis, aseptic meningitis, or encephalitis. Mumps and unidentified ECHO viruses were encountered with about equal frequency in nonparalytic poliomyelitis and aseptic meningitis (6 to 9%), but in cases of encephalitis mumps virus was identified more frequently (12%). Western equine encephalomyelitis, St. Louis type encephalitis, or herpes simplex viruses were identified in occasional cases of nonparalytic poliomyelitis and aseptic meningitis (2%) and only slightly more often in cases classified as encephalitis (7%). Since the mumps virus has been the most commonly recognized etiological agent in reported cases of encephalitis in California in recent years (unpublished data), it is of interest that Coxsackie viruses were encountered slightly more often than the mumps virus among the cases of clinical encephalitis in this study.

The less frequent occurrence of poliovirus infections and compensating increase in other viruses among vaccinated patients is also apparent in patients with nonparalytic poliomyelitis or aseptic meningitis. Among the group of encephalitis cases, however, in which a poliovirus could rarely be implicated, there was no evident pattern of difference in the laboratory findings with respect to vaccination.

In about one-half of the cases diagnosed as nonparalytic poliomyelitis, aseptic meningitis, or encephalitis, the combined efforts of stool and serologic examinations failed to reveal the presence of any current virus infection.

Comment

The diversity of viruses found in association with various clinical manifestations of C. N. S. disease points up the dilemma confronting alike the clinician, the virologist, and the epidemiologist, in attempting to determine causal relationships. The viruses detected in this study may each be widely distributed in the population at times, producing inapparent infections and minor illnesses, and to a variable extent are capable of invading the C. N. S. and giving rise to an overlapping spectrum of clinical syndromes.

The finding of Coxsackie or other nonpolioviruses in association with 5% or less of the paretic illnesses in nonvaccinated patients does not, in itself, indicate whether or not infection with these agents was merely coincidentally present or was the cause of illness. In view of the several well-documented reports[4] of paralytic disease in which enteroviruses other than poliovirus have been implicated as etiological agents, it appears reasonable to believe that the nonpolioviruses encountered among paralytic patients in the present study were the probable cause of illness in at least some instances. By separation of the cases regarded clinically as paralytic poliomyelitis into categories according to the doses of vaccine received, various illnesses which might be mistaken for poliomyelitis were, in effect, concentrated in the immunized group of patients. Hence, the marked increase in the association of nonpolioviruses with paralytic illness among the vaccinated patients, correlating with the number of doses of vaccine received, indirectly provides further substantiation of the etiological significance of these agents. These observations support recent predictions by Steigman[4a] and by Dalldorf[11] that widespread vaccination would make paralysis due to other viruses more conspicuous.

The clinical characteristics of the paralytic illnesses observed in this study which appeared to be attributable to nonpolioviruses will be described elsewhere. It should be noted, however, that the muscle paresis in illnesses associated with Coxsackie, unidentified ECHO virus, or mumps virus infection was almost uniformly graded as of slight or moderate severity. This was often, but less uniformly, true of the muscle gradings in patients in whom the laboratory evidence of poliovirus infection was negative, and no other agent was implicated. Cases clinically regarded as paralytic poliomyelitis in which supporting laboratory evidence of poliovirus infection was lacking have previously been noted by us[10] and by others.[12]

It is of interest that apart from vaccination status, the proportion of paralytic illnesses for which no etiological agent could be established became somewhat higher with increasing age.

Nonparalytic illness in patients who had received vaccine was also consistently less often related to poliovirus infection and more often associated with other viruses than in nonvaccinated patients. It appears evident that vaccination provided significant protection against all clinical types of C. N. S. disease due to poliovirus, including nonparalytic as well as paralytic illness. These findings confirm, and extend, those of Davis and Melnick.[1b]

The importance of Coxsackie viruses, ECHO viruses, and the mumps virus as causative agents of the nonparalytic poliomyelitis or aseptic meningitis syndrome requires little comment. In this study, clinical diagnoses of aseptic meningitis and nonparalytic poliomyelitis, as rendered by the attending physician, were examined separately, since, with few exceptions, the cases classified as nonparalytic poliomyelitis were entered in the official morbidity records of the local and state health departments as cases of poliomyelitis. In each of the three years of this study, poliovirus was recovered in less than one-fourth of the cases of "nonparalytic poliomyelitis" and the number of poliovirus isolations was exceeded by the number of Coxsackie virus isolations in two of the three years. This is striking evidence of the range of error in poliomyelitis morbidity statistics in recent years in California and other states in which nonparalytic cases, comprising some 30 to 50% of the reported cases, are included in the poliomyelitis incidence figures.

The finding that Coxsackie viruses were associated with illnesses clinically diagnosed as encephalitis more frequently than were mumps, herpes, or the arthropod-borne encephalitis viruses strongly suggests that Coxsackie viruses were the causative agent in some of these illnesses. Clinical histories, however, indicate that there was little to distinguish some of these illnesses from an aseptic meningitis syndrome other than slight drowsiness or lethargy. In other cases, convulsions and evident changes in sensorium were recorded. These observations add to previous reports[13] of association of Coxsackie and orphan viruses with encephalitic illness.

Viewed as a whole, the findings presented herein coupled with those of other investigators suggest that the viruses of the Coxsackie and ECHO group, like poliovirus and, to a lesser extent, the mumps virus, should be recognized as having protean pathogenic capabilities enabling them to give rise to a broad spectrum of syndromes of the central nervous system, embracing the clinical picture of aseptic meningitis, mild to moderate paralytic poliomyelitis, meningoencephalitis, and encephalomyelitis.

Several reasons may be advanced to account for the high proportion of cases of acute C. N. S. disease for which an etiology was not determined by the present study: 1. The laboratory procedures sometimes failed to detect infections for which examinations were made. 2. Illness was due to known infectious agents for which tests were not made. 3. Illness was often due to etiological factors, infectious and/or noninfectious, which are not yet recognized. In our opinion, it is probable that the first two reasons were contributory but that other etiological factors must still be sought to account for the high proportion of acute illnesses of the central nervous system which elude definitive laboratory diagnosis.

Summary

Viral laboratory studies were carried out in a series of 1,407 patients admitted to hospitals in California with suspected viral disease of the central nervous system during 1955, 1956, and 1957. Among patients given a clinical diagnosis of paralytic poliomyelitis who had not received poliomyelitis vaccine (Salk type), poliovirus was recovered more frequently (81%) from those under 5 years of age than from those in older age groups (60 to 64%). In each age group, the recovery of poliovirus was markedly lower among vaccinated patients, being successful only one-half to one-third as often among those who had received two or more doses of vaccine as among those who had received no vaccine or only one dose.

The results of virus isolation attempts were supported by complement-fixation tests, which only occasionally revealed a significant rise in antibody titer in patients whose stools failed to yield a poliovirus. Laboratory evidence of other viral infections associated with cases of clinical paralytic poliomyelitis included Coxsackie viruses, group B (types 2 to 5) and group A (type 9); ECHO viruses; mumps virus; and epidemic (St. Louis type) encephalitis and herpes simplex viruses. These agents were found much oftener in vaccinated patients, with a frequency equal to that of proved poliovirus infections among the two-dose vaccinees. The muscle paresis associated with nonpoliovirus infection was almost uniformly of mild to moderate severity.

Among illnesses clinically classified as nonparalytic poliomyelitis or aseptic meningitis, poliovirus infection was demonstrated in less than one-fifth of the nonvaccinated patients and was consistently less often established in those who had received the vaccine. The same array of nonpolioviruses was

encountered, the most frequent of which were the Coxsackie group B viruses. No etiological agent was established in about one-half of the cases.

In cases clinically classified as encephalitis, no single agent was found in more than 15% of the group and no virus could be implicated in slightly more than one-half of the cases. Coxsackie viruses and the mumps virus were somewhat more frequently identified than were the other agents, viz., the western equine encephalomyelitis, St. Louis type encephalitis, herpes simplex, poliomyelitis, and unidentified ECHO viruses. In each clinical category, 1 to 3% of the patients had evidence of concurrent infection with two viral agents.

These data provide additional evidence of the protective effect of inactivated poliovirus vaccine against both paralytic and nonparalytic illness due to poliovirus infection. They also illustrate how the suppression of poliomyelitis by widespread vaccination makes more conspicuous the occurrence of paralytic poliomyelitis-like illnesses due to other causes.

2151 Berkeley Way (4) (Dr. Lennette).

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TOXICITY OF FERROUS SULFATE.—It is now clearly evident that the accidental ingestion of over-dosages of therapeutic iron preparations may be fatal to children. As little as one gram of ferrous sulfate is now considered to be a potentially fatal dose. The data . . . indicate that the toxicity of iron may be more closely related to the systemic effects induced by absorbed iron than to localized traumatic effects of the iron upon gastrointestinal tissues. In experimental animals toxicity and death appear to be directly associated with the serum iron rises during the first few hours subsequent to the oral administration of iron in aqueous solution. —H. Albert, C. R. Kemp, and W. G. Rohse, American Physiological Society Proceedings, Fall Meeting—Sept. 8-11, 1959, *The Physiologist*, August, 1959.

CHOICE OF ANESTHETIC TECHNIQUE IN COMPLICATIONS OF PREGNANCY AND LABOR

David M. Little Jr., M.D.
and
William K. Bannister, M.D., Hartford, Conn.

There are no pat formulas for anesthesia in obstetrics. The anesthesiologist must understand not only the possible complications of pregnancy and labor but also the manner in which the individual obstetrician intends to deal with such complications as may arise. Classification and review of the complications inherent in the products of conception, maternal complications, and complications of delivery show how important it is to be discriminating in choosing between general and regional anesthesia, in deciding on the level of general anesthesia, and in using relaxants. Experience has led to the recognition of certain basic situations for which rational methods of anesthetic management have been developed, and the tendency to settle down to routines of single anesthetic methods to the exclusion of all others should be resisted.

When anesthesia first came into use there was only ether, and the choice was simple; for, as Liston asserted, "This Yankee dodge beats mesmerism hollow." Today, 112 years after Sir James Simpson administered the first obstetric anesthesia on Jan. 19, 1847, the decision has become immeasurably more difficult. The entire gamut of anesthetic agents and techniques has been employed in a vain search for the ideal obstetric anesthetic procedure which would be suitable for all patients under all circumstances. It now seems clear that there is no such ideal. The search, however, has produced many champions of individual drugs and many advocates of specific methods. There is, at present, a growing tendency among certain obstetricians, anesthesiologists, and even whole lying-in clinics to employ and extol, to the exclusion of all others, a single anesthetic agent or technique for use in obstetrics. Indeed, the words "routine" and "always" are becoming almost the hallmark of the literature on obstetric analgesia and anesthesia.

The administration of obstetric anesthesia is hazardous at best, for there are two patients to be considered and two lives to be sustained. When either pregnancy or labor is complicated or in any way abnormal, the hazards are increased. Certain of these complications of pregnancy and labor constitute definite indications for one type of anesthetic procedure and definite contraindications to the employment of others. The use of the wrong agent or technique in such an instance, however well-conducted the anesthesia may be, must surely represent a barren triumph of technique over reason. The anesthesiologist not only must be aware of the nature of these complications of pregnancy and labor but also must understand the manner in which the individual obstetrician with whom he is associating intends to deal with such complications. Furthermore, consideration must also be given to the effect of anesthesia on the pathological process involved as well as on the operative procedure that is contemplated.

It would be at least equal sophistry to suggest that there exist pat formulas or rules of thumb designed to cover all the various obstetric situations and exigencies. Obviously there are not. There are, however, certain basic situations for which rational methods of anesthetic management have been evolved on a sound, physiological basis.

Complications Inherent in the Products of Conception

Extrauterine pregnancy occurs about once in every 300 gravid women. The danger of hemorrhage, shock, and collapse, as the chorionic villi burrow their way into blood vessels and through the tubal wall, requires a mode of anesthesia designed to protect the patient in the event of such an accident. For this reason, the patient's compensatory cardiovascular reflexes must not be transgressed, and such anesthetic methods as spinal and caudal, which accomplish sympathetic blockade and thus rob the body of much of its ability to produce compensatory vasoconstriction, must be avoided. Very light general anesthesia is indicated in these instances, with the addition of muscle relaxants to the basic inhalation techniques, when muscle relaxation becomes necessary. Obviously, these patients are candidates for emergency operative intervention, and the problem of the full stomach introduces itself. When both anticipated hemorrhage and a full stomach confront the anesthesiologist, the only safe anesthetic management would appear to be the introduction of a cuffed endotracheal tube, with the patient awake and in control of her laryngeal reflexes, followed by light general

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From the Department of Anesthesiology, Hartford Hospital.

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anesthesia, preferably induced with cyclopropane. Muscle relaxant drugs may then be added as necessary.[1]

Two other complications involving the products of conception, namely, placenta previa and premature separation of the placenta, can lead to hemorrhage, shock, and death. Danger to the fetus is especially high when its circulation is compromised by separation of the placenta. The incidence of placenta previa is about one in 500 cases and of premature separation about one in 300 cases. For reasons already noted spinal, caudal, and epidural anesthesias must be avoided. At the same time the hypoxic fetus should not be subjected to the depressant effects of strong general anesthetic agents. Pudendal block or very light general anesthesia are the best choices for relief of pain during vaginal delivery. If cesarean section is elected because of massive hemorrhage before labor has progressed far enough for vaginal delivery, light general anesthesia supplemented by a muscle relaxant is the logical technique. It should be unnecessary, although perhaps wise, to add that high concentrations of oxygen are always indicated in obstetric anesthesia and particularly in all instances of hemorrhage in which a high partial pressure of oxygen may compensate to some extent for the lowered oxygen-carrying capacity of the blood.

Premature labor, on the other hand, requires a different anesthetic approach. Prematurity of the fetus has a hospital incidence of 3.2%, and therefore is one of the most common complications of the pregnant patient who receives anesthesia. All else being equal, the anesthetic management must be devised to avoid depression of the fetus. Clifford [1A] has pointed out that the premature infant is easily narcotized with either medicaments or general anesthetic agents and that the two in combination are frequently lethal. It is essential that medication be restricted to the minimum compatible with the maternal pain threshold and that some form of regional anesthesia be chosen: local infiltration, direct nerve block, caudal, epidural, or spinal analgesia. All these, when properly conducted, should spare the premature infant from further depression and are much preferable to the general anesthetic agents, with their ability to produce transplacental narcosis.

Maternal Complications

Without the shadow of a doubt, the most common and important maternal complication from the viewpoint of the anesthesiologist is that of a full stomach at the time of delivery. Since obstetric anesthesia is emergency anesthesia, insofar as the patient is unprepared, obstetric patients frequently come to delivery with a full, or partially full, stomach. Furthermore, it is well established that the gastric emptying time is much prolonged by both labor and the sedative drugs often employed during labor, so that the stomach may still contain food ingested 8, 12, or even 16 hours prior to delivery.[2] The incidence of frank emesis of these stomach contents has run as high as 40% in some series of obstetric anesthesias,[2] and even in the absence of active vomiting a silent regurgitation of gastric juice may occur and produce a form of bronchopneumonia.[3] It is clearly the duty of the anesthesiologist to protect the patient who comes to delivery with a full stomach, and some form of regional anesthetic technique is mandatory. Merrill and Hingson [4] believe that either locally or caudally induced analgesia are the choices, since they have reported vomiting and aspiration of vomitus even with spinal anesthesia. However, few others would dispute that spinal anesthesia, if not the preferred method, is at least many times better than general anesthesia in any form. The aspiration of vomitus is now a leading cause of obstetric deaths related to anesthesia,[5] the incidence of aspiration itself being 0.15% in one hospital series of 44,016 pregnancies [6] and accounting for 51% of 59 maternal deaths in another investigation.[4] It is obviously the obligation of all physicians to protect their patients from this thoroughly preventable tragedy. Therefore, when general anesthesia is absolutely indicated in the patient with a full stomach, it is mandatory to insert a cuffed endotracheal tube while the patient is awake and in control of her laryngeal reflexes prior to inducing the general anesthesia.

The toxemias of pregnancy, preeclampsia and eclampsia itself, apparently have the same underlying, although as yet unknown, pathogenesis; but they present different problems from the point of view of anesthesia. Preeclampsia has an incidence of about once in every 20 deliveries, while true eclampsia occurs about once in every 500 pregnancies, in lying-in practice. The milder toxemias, or preeclampsias, present evidence of metabolic upset and parenchymal damage, and anesthetic agents which are known to produce further profound metabolic upset, such as ether, chloroform, vinyl ether (Vinethene), ethyl chloride, and even trichlorethylene, should be avoided. Here is an indication for those regional procedures such as spinal and caudal analgesia, which not only leave the body metabolism relatively unaffected but further produce some degree of sympathetic blockade. When true eclampsia occurs, with convulsions and coma in addition to the parenchymal damage already referred to, the indication is again for some form of regional anesthesia, often merely local infiltration, with intravenous administration of thiopental (Pentothal) sodium as needed to control the convulsions.[7]

Serious heart disease during pregnancy occurs in approximately 2% of clinic patients but ranks high on the list of causes of maternal death. Heart disease of even the mildest type is a distinct hazard when complicated by pregnancy, and the care of such patients, particularly the choice of analgesia and anesthesia, deserves detailed consideration. The danger of decompensation is very real and increases in proportion to the strain placed on the myocardium by the burdens of labor and delivery. The aim must therefore be to prevent all such strain, either physical or emotional, and to shorten the second stage of labor as much as possible. In this regard, the use of continuous caudal or spinal anesthesia throughout labor and delivery has proved to be an excellent solution to the entire problem. There are those patients, however, on whom regional procedures must not be forced, since they are capable of doing more harm than good by virtue of the emotional strain produced; for such patients good sedation throughout the first stage of labor, and the use of a terminal regional procedure or perhaps light general anesthesia, must be the choice.[8] In the face of frank decompensation a regional procedure must be employed, and under such circumstances spinal anesthesia has the great advantage of producing a bloodless phlebotomy and thus becomes the indicated anesthetic procedure.[9]

Until the advent of insulin diabetic women were usually sterile, so that this disease was an infrequent complication of pregnancy. Today, the incidence of diabetes is still not high, being only 0.174% in one series of 31,544 deliveries[10]; but the problems it presents from the anesthetic point of view are important, inasmuch as there is a marked increase in the incidence of both hydramnios and toxemia in the pregnant diabetic, and the stillbirth and neonatal death rates are appreciably increased. The preferred anesthesia is therefore some form of conduction anesthesia, either caudal, epidural, or spinal. This approach will serve to protect the infant from the hazards of systemic narcosis, while at the same time it will not alter the functional activity of the maternal pancreas, thus permitting more adequate control of the problems of both maternal and infant acidosis.

Finally, there are two types of pregnant women who demand special classification as far as anesthetic treatment is concerned. The first is the elderly primipara. In such a patient, the increased value of the fetus to the parents, together with the increased frequency of dystocia, requires that the case be treated as is prematurity. Heavy premedication and deep general anesthesia should be avoided and preference should be given to caudal, epidural, or spinal anesthesia or some other type of regional procedure. If general anesthesia must be used, the plane of anesthesia should be kept as light as is compatible with the exigencies of delivery.

The other problem mother is the "dangerous multipara," or the "grande multipara." Such women are apt to have excessively succulent tissues, and the danger of hemorrhage from even small tears and lacerations is great. For this reason such techniques as spinal or caudal induction of anesthesia, which produce sympathetic blockade and hence the loss of the compensatory cardiovascular reflexes, are best avoided if possible. However, it must also be remembered that the incidence of asphyxia neonatorum increases after the eighth delivery, so that, again, general anesthesia, if employed, should be kept at a light level. Perhaps the most enlightened choice of anesthesia in such instances would be local infiltration, with a vasoconstrictor substance added to the local anesthetic solution.

Complications of Delivery

Certain abnormalities of position and presentation of the fetus also complicate labor, and therefore delivery, and demand special attention to the anesthetic requirements for delivery. Breech presentation, for instance, occurs in about 4% of all pregnancies, and the three varieties of breech presentation offer differing anesthetic problems. In the case of a full or a frank breech presentation, intrauterine manipulation necessitates the use of deep ether, chloroform, or vinyl ether anesthesia to provide uterine muscle relaxation, which cannot be facilitated and may even be decreased by the use of regional anesthetic procedures, such as spinal or caudal, which produce sympathetic blockade and therefore parasympathetic predominance. In a footling presentation per se, on the other hand, or when either a full or frank breech has been converted to a footling presentation by intrauterine manipulation, the problem is different: the need is for perineal relaxation and minimal further trauma to the fetus in the way of depressant drugs. Therefore, in a footling presentation per se, spinal, caudal, epidural, or light general anesthesia, with a supplementary muscle relaxant agent for perineal relaxation, all serve adequately; in the converted frank or full breech presentation, the general anesthesia may be greatly lightened for actual extraction and a muscle relaxant employed for further perineal relaxation.

Occipitoposterior positioning occurs in about 20% of vertex presentations, but the incidence of its persistence during labor, which demands particular anesthetic management, is considerably less frequent. Persistent occipitoposterior positioning presents a situation that exemplifies well the fact that the anesthetist not only must be aware of the nature of the existing complication of pregnancy or labor but also must understand the manner in which the individual obstetrician with whom he is associating intends to treat such complications. Many obstetricians, when faced with a persistent occipitoposterior position, will elect to perform a Scanzoni maneuver if the head is on the perineum but will do a manual rotation if the vertex remains higher in the birth canal. A Scanzoni maneuver will require the perineal relaxation afforded by spinal, caudal, or general anesthesia supplemented with a muscle relaxant drug; on the other hand, manual rotation frequently demands that uterine muscle relaxation be obtained, and deep anesthesia with use of ether, chloroform, or vinyl ether may well be necessary.

Transverse arrest presents a somewhat similar problem. Additional fetal trauma in the form of deep anesthesia must be avoided, yet the danger of tears requires that the maternal soft tissues and perineal muscles be well relaxed. For these reasons, spinal or caudal analgesia provide a solution, which can also be provided by the use of light general anesthesia, with the additional administration of a muscle relaxant agent.

Brow and face presentations are relatively rare, occurring in 0.17 and 0.38%, respectively, of labors. The problem is, again, to secure sufficient perineal relaxation for operative delivery from below, without subjecting the fetus to further depression, and so deep general anesthesia should be avoided. Once again, spinal or caudal analgesia, or light general anesthesia with the additional use of a muscle relaxant, will serve the purpose well.

Summary

The high incidence of complications during pregnancy, labor, and delivery demands special anesthetic management for each complication. When hemorrhage and shock are encountered light general anesthesia is indicated, with supplemental muscle relaxation when necessary. Fetal immaturity and maternal metabolic diseases are usually indications for the use of a regional anesthetic. Abnormal fetal presentations may require deep general anesthesia for uterine relaxation or either spinal blockade or general anesthesia supplemented by muscle relaxants for perineal relaxation. The dangers of vomiting and aspiration of vomitus must always affect the choice and management of general anesthesia for obstetric procedures.

80 Seymour St. (15) (Dr. Little).

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THE LENS IN DIABETES.—A sudden alteration in the volume of the lens is a frequent finding among diabetics, and this necessarily causes a change in refraction, which may be very transient, but is sometimes very dramatic. The lens capsule is semipermeable, so in the acute stage of diabetes the fluid content of the lens promptly increases, and myopia ensues; but as soon as diet or insulin have controlled the hyperglycemia, the process is reversed, the lens shrinks, the myopia is shed, and several degrees of hypermetropia may even result. The unstable diabetic will thus have an equally unstable focal range, and such patients must be sight-tested only at periods of a balanced blood-sugar, or the spectacles will be far from correct. . . . The true Diabetic Cataract occurs only in youth, generally between the age of 15 and 25, but exceptionally in infancy; and it is remarkable for its rapidity, the whole lens becoming opaque within a few weeks in adolescence, or within a few days in children. Its development is roughly proportional to the severity of the diabetes. . . . A simple senile cataract arises in the elderly diabetic with slightly greater frequency than in the population at large. Such lens opacities often start beneath the posterior capsule, with a brassy iridescence reminiscent of the more brilliant "polychromatic lustre" in "complicated" cataracts (i.e. secondary to a uveitis) which similarly start beneath the posterior capsule.—P. D. Trevor-Roper, M.A., M.B., B. Chir., The Ocular Complications of Diabetes, *The Postgraduate Medical Journal,* May, 1959.

EFFECT OF POLLUTED LOS ANGELES AIR (SMOG) ON LUNG VOLUME MEASUREMENTS

Hurley L. Motley, M.D., Reginald H. Smart, M.D.
and
Charles I. Leftwich, M.D., Los Angeles

The breathing of smog has direct effects on the respiratory tract in addition to direct effects on the eyes and indirect statistical effects on total mortality. The direct respiratory effects were studied in 66 volunteers, 46 of whom had pulmonary emphysema. Measurements were obtained of total vital capacity, timed vital capacity, maximal breathing capacity, residual air, and rate of nitrogen-washout during oxygen breathing. These were used as criteria for the improvement noted when subjects, after breathing either smoggy air or clear Los Angeles air, were allowed to breathe air filtered through activated carbon. The most significant improvement found was the decrease in the volume of residual air noted when subjects with emphysema breathed filtered air for not less than 40 hours. The severity of emphysema was aggravated by smog. No significant changes in lung volume measurements were demonstrated from the breathing of filtered air as compared to smoggy air by essentially normal subjects.

The health effects of air pollution are of great interest throughout the world at present. Although the eye-irritating effect of smog is often obvious in the Los Angeles area, the presence of a significant deleterious effect on breathing has not been so generally recognized. A number of clinicians in the Los Angeles area have attributed to air pollution increasing severity of symptoms in persons with chronic pulmonary disease such as emphysema and asthma or in other chronically ill patients. These opinions are based largely on the subjective symptoms of patients in relation to the air breathed and to atmospheric conditions. Elderly persons with chronic pulmonary and cardiac disability appear to suffer the most severe effects. Acute illness of an epidemic proportion has occurred from air pollution in the past, as in the Meuse Valley in Belgium in 1930,[1] in Donora, Pa., in 1948,[2] and in London in 1952 and 1956.[3] Persons with chronic pulmonary disease were the most severely affected, and many died, although the normal population also suffered from eye irritation, coughing, wheezing, chest pains, nausea, and vomiting.

The composition of smog in Los Angeles is different in certain respects from that found in other parts of the United States such as St. Louis, Pittsburgh, or New York. There is an absence of coal smoke in Los Angeles, and the location of the city in an area hemmed in by mountains on three sides with the sea on the fourth results in less breeze and permits inversions of the atmosphere with the occurrence of smog. The operation of 3 million automobiles is the major source of smog[4] in Los Angeles. The automobile exhaust contains carbon monoxide, hydrocarbons (organic vapors), olefins, oxides of nitrogen, aldehydes, oxides of sulfur, and particulate matter. Smog results from chemical reactions among the pollutants. Hydrocarbons are oxidized in the presence of sunlight, with nitrogen dioxide acting as a catalyst, and ozone is formed. Aerosols result from particles of solids or liquids becoming highly dispersed, and these scatter light waves, reducing visibility. Adsorption of oxidants to aerosols may intensify the irritant effects of smog. Industrial pollution consists primarily of organic solvent emissions and residues from fuel-oil burning, such as oxides of nitrogen, carbon monoxide, sulfur oxides, and particulate matter. The chemical composition of the air pollutants is complex, including many unstable chemical compounds, especially in the presence of sunlight.

Smog alerts are called by the Los Angeles Air Pollution Control District (LA-APCD) on the basis of the attainment of designated levels of four constituents of smog; namely, ozone, oxides of nitrogen, sulfur dioxide, and carbon monoxide. Thus far, alerts have been called only for ozone, and most of these have been of relatively short duration, some for only a few minutes. The high concentration is often present at only one of the sampling stations in the Los Angeles area (a first-stage alert is called when the ozone level reaches 0.5 ppm).

The major health problem at present relates to the effects of the pollutants in the atmosphere at lower concentrations than the alert level and for prolonged periods of time. Other constituents of smog may be more harmful than the four pollutants used as criteria for calling alerts. Haagen-Smit[5] reports that chromatographic and spectrographic

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From the Cardio-Respiratory Laboratory, University of Southern California School of Medicine. Dr. Leftwich was Research Fellow in Cardio-Respiratory Laboratory, from the state of California, Department of Public Health, 1955-1956.

analysis of Los Angeles smog revealed the presence of many aldehydes and organic acids and of a multitude of hydrocarbons. The composition of smog changes from hour to hour at any given location. The use of synthetic smog mixtures in studying the effects on man presents many problems. Reproduction of the same response as the naturally occurring air pollution in this area would require maintenance of the same composition of pollutants, variations of concentration in the environment, time of exposure, and photosynthesis. Kotin and Falk[8] report that an artificial smog made by reacting gasoline and ozone in realistic oxidant concentrations produces no demonstrable physiological or morphologic changes in presumably healthy animal species. Even with oxidant concentrations of 30 times the average concentration on a smoggy day, the physiological changes are all of a low order of magnitude and rapidly disappear after removal of the animal from exposure. Studies on a limited number of healthy human volunteers revealed no significant physiological change after acute short exposure to realistic oxidant concentrations of a synthetic smog made from gasoline and ozone.

TABLE 1.—*Number of Patients in Three Exposure Groups, by Condition*

Condition	Exposure Group*		
	Short (2-4 Hr.)	Moderate (18-20 Hr.)	Prolonged (40-90 Hr.)
Pulmonary emphysema	15	13	18
Bronchiectasis	1	1	2
Bronchial asthma	1	2	1
Chronic bronchitis	1	1	0
Pneumoconiosis	1	1	0
Postpneumonectomy	1	1	0
Cystic disease of the lung	0	0	1
Sarcoidosis	0	1	0
Exposure to chemical fire	0	0	1
Cardiac disease	0	0	1
Normal	1	0	1
Total	21	20	25

* Short-exposure group: age range 19 to 66 yr., room temperature 22 to 28 C (av. 24); moderate-exposure: age 50 to 70 yr., temperature 21 to 28 C (av. 23); prolonged-exposure: age 26 to 71 yr., temperature 20 to 28 C (av. 24.5).

As a result of proposals to change the "first alert" level to a higher value than 0.5 ppm of ozone, tests were made in which a volunteer was exposed to about 2 ppm of ozone in an outside chamber. A significant impairment in respiration, as shown in the spirogram measurements[7] (especially the timed vital capacity for three seconds and the shape of the exhalation curve), resulted from this short-term exposure to the high concentration of ozone. The alert level for ozone was not raised, and there has been no further discussion on this aspect after this one test.

The primary purpose of the present study was to obtain objective quantitative lung volume measurements on human subjects, particularly those with pulmonary insufficiency, while they were breathing air during the smoggy periods that naturally occur in Los Angeles and then to compare the changes in pulmonary function which might be induced by breathing air which had been filtered to remove smog. The question we sought to answer was whether the breathing of smoggy air produces a significant deleterious effect which can be measured by pulmonary function tests.

Procedures

These studies have been carried out over the past three and one-half years. The number of studies which could be performed with this procedure was limited because of the problem of availability of suitable subjects for study during smoggy periods and during an additional two-or-three-day stay in the filtered-air room in the hospital. Residence in this room was somewhat monotonous for many of the subjects. All studies were carried out at the University of Southern California cardiorespiratory laboratory, located on the second floor of the Hospital of the Good Samaritan near the downtown section of Los Angeles. Smog, when present in the Los Angeles basin, is quite prevalent in the hospital area. The central monitoring station of the LA-APCD is in this general area, so that the approximate readings for ozone, oxides of nitrogen, sulfur dioxide, and carbon monoxide can be obtained daily. The intensity of smog varies in different parts of the Los Angeles basin from day to day, and the area of the laboratory represents an average, having a concentration less severe than some but more severe than other locations.

The filtered air was obtained with use of activated carbon filters (Pure Air Type, model A-5, 42 lb. of carbon per filter and 500 cu. ft. of air flow per minute). It has been shown that air filtered over activated carbon protects plants[8] in greenhouses, and plants are very sensitive to even low concentrations of smog. Lung function measurements were obtained and compared while subjects were breathing both the smoggy air and the filtered air at the same study period. (The subjects were kept for from 2 hours to as long as 90 hours in the filtered-air room.) Each person was used as his or her own control. This procedure enhanced the validity of attributing the changes in pulmonary function measurements to air pollution rather than to some other factor. Periodic variations in lung function measurements do occur in the absence of air pollution in patients with severe chronic pulmonary disease, such as emphysema, especially during respiratory infections. Every attempt was made to make the only variable in the study the atmosphere which the subject breathed. The room temperature ranged from 20 to 28 C, and in a similar degree for the three groups studied (table 1).

Air was classified as smoggy when there was a definite odor of ozone, reduced visibility, eye irritation, and the prediction of smog by the LA-APCD, including reports of the pollutants from the monitoring stations. The general procedure was to obtain subjects for study after they had been exposed to smoggy periods of at least three to four days' duration and to obtain the initial lung volume measurements. The subjects studied and the data reported for clear air in Los Angeles represent a period of more than three days of no smog forecast by the LA-APCD, no odor of ozone, no evidence of eye irritation, and good visibility.

The maximum concentration of the various air pollutants reported as being present between 9 a. m. and 2 p. m. by the LA-APCD downtown station during the days of the studies is given below. Concentrations of total oxidants ranged from 0.2 to 0.7 ppm, with ozone from 0.20 to 0.53 ppm, oxide of nitrogen from 0.2 to 0.6 ppm, sulfur dioxide from 0.05 to 0.25 ppm, and carbon monoxide from 5 to 27 ppm. The absence of the eye-irritating property of smog and of the odor of ozone has been consistently noted by subjects while breathing filtered air, even for a few minutes. The odor of ozone was often quite apparent when one left the filtered-air room, even on some days when the LA-APCD reported no significant smog and permitted incinerator burning, before the latter practice was banned in this city. These studies have not been correlated with concentrations of individual constituents of air pollution but rather with the presence or absence of smog.

Three major time intervals in the filtered-air room were used: (1) a short duration of 2 to 4 hours, (2) a moderate duration of 18 to 20 hours, and (3) a prolonged duration with a minimum time of 40 hours and a maximum of 90 hours (average, 55 hours). The short runs of two to four hours were compared on the same day, with the subject first breathing the smoggy air and then filtered air, or breathing clear Los Angeles air then filtered air. All of the other subjects, who were kept in the filtered air for moderate or prolonged periods, were admitted to the hospital and after the initial study were kept continuously in the room with the activated carbon filter.

Material for Study

All of the subjects studied were volunteers, and they were willing to reside in the filtered-air room for varying lengths of time, including the time necessary for repeat measurements of lung volume. The subjects included 16 women and 50 men (ages 19 to 71 years), and 46 of the 66 had pulmonary emphysema (table 1). Subjects with severe emphysema were sought because of their diminished breathing reserve and a greater likelihood that changes induced by breathing the smog air would be detectable. Most of the subjects did not desire or would not volunteer to have a repeat arterial puncture within one to two days after having an initial puncture and did not want to swallow the esophageal balloon for the compliance measurements.

Fatigue was one of the difficulties complained of on the short run of two to four hours' duration, especially in the patients with severe emphysema, since all of the tests were performed on the same day. Close checks were required for the residual air measurements, and several measurements were frequently necessary to obtain the accuracy desired. Satisfactory measurements were obtained in all subjects at both study periods, and, so far as is known, the air breathed was the only variable.

Measurements

Measurements were obtained of total vital capacity, timed vital capacity for three seconds, and maximal breathing capacity on the 13½-liter Collins respirometer.[9] The spirogram tracing was recorded with the fast speed so that the shape of the exhalation curve, the exhalation time, and evidence of air trapping, when present, could be noted. Bronchospasm was evaluated by measuring changes in the maximal breathing capacity after the administration of a bronchodilator treatment with either isoproterenol (Isuprel) or racemic epinephrine (Vaponefrin).

The amount of residual air was measured by both the oxygen open-circuit and the improved helium closed-circuit [10] methods and was checked routinely by repeat measurements for values not to exceed 100 ml., or, in the subjects with severe emphysema, the residual percentage of total lung capacity not to exceed 2%. Measurement of expiratory reserve was obtained at the time of each residual air measurement, as this permitted determination of the precise level of the diaphragm at the time and improved the accuracy of the residual air measurement.[10] The volume of the residual air as observed in chronic lung disease varies widely from less than 40% of the normal predicted in pulmonary fibrosis to over 400% in pulmonary emphysema.

The ventilation factor [11] was used to evaluate the ability to use the chest and lungs as a bellows. This value was obtained from the average of the timed vital capacity for three seconds, the maximal breathing capacity, and the residual percentage of total lung capacity, all expressed on a basis of 100% of the normal predicted. All of the lung volume measurements were expressed at body temperature and at ambient and saturated barometric pressure. All of the residual air measurements were obtained with the patient in the fasting state and lying supine.

Air distribution in the lungs was studied by means of the nitrogen meter, with continuous recordings of each breath during oxygen breathing. The oxygen breathing was continued until an end tidal nitrogen concentration of 1% was reached, unless more than 15 minutes was required. Extensive studies have been performed to evaluate the nitrogen washout test with the nitrogen meter.[12]

The nitrogen washout curve is quite reproducible and provides significant information for evaluating pulmonary function impairment. However, the method of using a single deep breath of oxygen with the nitrogen meter was found unsatisfactory for quantitative comparisons in this study. The single-breath nitrogen curve was not consistently reproducible in the same subject, and other studies indicated that this test reflected primarily the better ventilated alveoli.[13] The alveolar nitrogen content after seven minutes of oxygen breathing also provided additional information on the uniformity of air distribution in the lung.

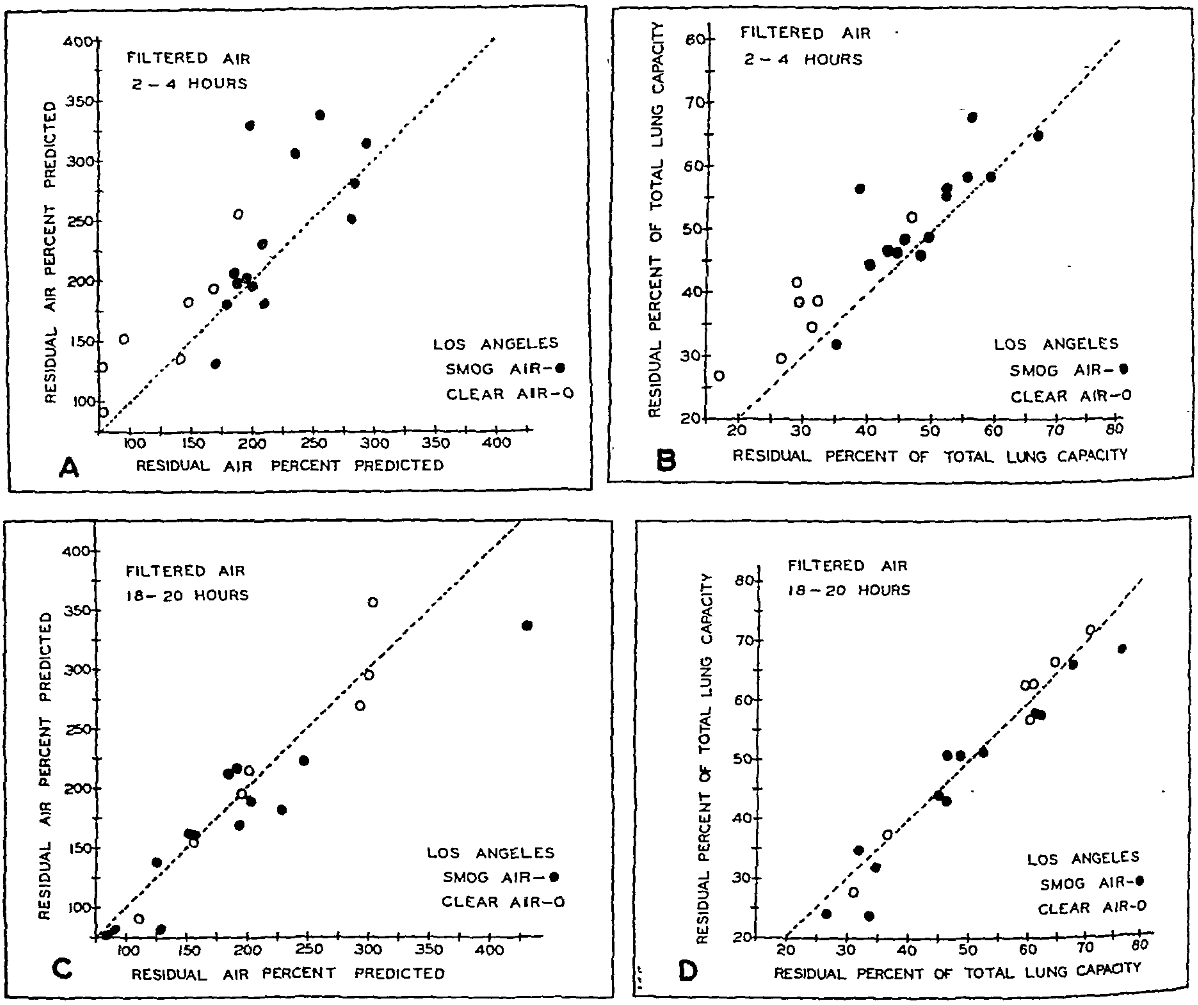

Fig. 1.—Comparison of volume of residual air as percentage of normal predicted and volume of residual air as percentage of total lung capacity in subjects breathing filtered air (ordinates) and Los Angeles smoggy air or clear air (abscissae) in 2 to 4 (*A*, *B*) and 18 to 20 (*C*, *D*) hours.

Results

The absolute volume of the residual air as a percentage of the normal predicted was determined in 14 subjects while they were breathing Los Angeles smoggy air and compared to the measurements after they had breathed filtered air for two to four hours. In seven subjects the comparison was made between breathing of Los Angeles clear air (nonsmoggy period) and breathing of filtered air for two to four hours. There was no significant difference between the results from smoggy and nonsmoggy periods (fig. 1*A*). The average percentage of residual air for the 14 subjects during the smoggy period was 220.4% as compared to 239.8% after two to four hours in the filtered-air room (table 2). In the seven subjects studied during the nonsmoggy period of breathing Los Angeles air, the average was 122.1% as compared to 152.6% after breathing of the filtered air. The volume of residual air as a percentage of total lung capacity increased after breathing of filtered air for two to four hours—52.5% as compared to 48.2% for smoggy air (fig. 1*B*). The seven subjects studied during nonsmoggy periods also showed a similar change in average percentage of total lung capacity—35% for filtered air and 29.4% for smoggy air.

The total vital capacity, timed vital capacity for three seconds, maximal breathing capacity, and ventilation factor measurements revealed, on an average, decreases after two to four hours' exposure to the filtered air (table 2). The alveolar nitrogen concentration showed no significant change after subjects had breathed oxygen for seven minutes. The results of the short exposure reveal no significant difference between smoggy and nonsmoggy periods, and the lung volume measurements, on the whole, showed definitely more impairment after subjects breathed the filtered air. Spirograms were obtained on 10 normal subjects (aged 22 to 34 years), employees of the laboratory or the hospital, during smoggy and nonsmoggy periods. Spirograms were again made after the subjects breathed filtered air for two to four hours, and no significant changes were noted. These data were not included in table 2, since the volume of residual air was not measured.

TABLE 2.—*Effect of Type of Air Breathed on Lung Volume Measurements in Six Exposure Groups**

	A		B		C		D		E		F	
Determinations	Smog†	Filtered‡ (2-4 Hr.)	Clear§	Filtered (2-4 Hr.)	Smog	Filtered (18-20 Hr.)	Clear	Filtered (18-20 Hr.)	Smog	Filtered (40-90 Hr.)	Clear	Filtered (40-66 Hr.)
Vital capacity (supine)												
Observed, ml.	3,328	3,044	3,939	3,808	2,537	2,584	2,532	2,460	3,143	3,318	3,699	3,535
% of predicted	83.6	76.5	83.2	80.4	68.6	69.9	71.4	69.3	79.9	84.3	90.0	86.0
Timed vital capacity (3 sec.)												
Observed, ml.	2,191	1,963	3,493	3,192	1,925	1,921	1,494	1,395	2,171	2,360	2,375	2,455
% of predicted	57.2	51.2	73.6	67.3	52.8	52.7	43.7	40.8	55.5	60.3	58.3	60.3
Maximal breathing capacity												
Observed, liters/min.	48.5	45.3	105.5	101.9	47.0	47.0	30.8	29.4	55.6	60.0	66.3	62.1
% of predicted	43.3	40.4	70.6	68.2	44.7	44.7	32.1	30.6	47.9	51.7	52.3	49.0
Alveolar nitrogen value after 7 min. of breathing oxygen, %	6.83	6.59	2.20	2.68	5.01	5.30	6.86	6.95	3.29	2.50	1.29	1.16
Residual air												
Observed, ml.	3,097	3,369	1,641	2,051	2,571	2,318	3,412	3,455	2,970	2,540	2,642	2,694
% of predicted	220.4	239.8	122.1	152.6	185.2	167.0	224.8	227.6	203.4	173.9	184.7	188.3
As % of total lung capacity	48.2	52.5	29.4	35.0	50.3	47.3	57.4	58.4	48.6	43.4	41.7	43.2
Ventilation factor, %	50.4	46.5	75.4	67.4	52.4	53.5	43.9	43.0	54.1	59.6	57.8	57.0

*Group A: 14 subjects (2 women), av. age 59 yr., av. calculated body surface area 1.75 sq. m.; group B: 7, 30 yr., 1.86 sq. m.; group C: 13 (6 women), 58 yr., 1.72 sq. m.; group D: 7 (2 women), 64 yr., 1.71 sq. m.; group E: 22 (5 women), 55 yr., 1.75 sq. m.; group F: 3 (1 woman), 53 yr., 1.86 sq. m.

†Smog: breathing Los Angeles air during smoggy periods.

‡Filtered: breathing air filtered over activated carbon to remove smog.

§Clear: breathing Los Angeles air during nonsmoggy periods.

The volume of residual air as percentage of the normal predicted was compared in 13 subjects breathing the Los Angeles smoggy air (185.2%) and after breathing of filtered air for 18 to 20 hours (167.0%). In seven cases the comparison was made after breathing of Los Angeles clear air (224.8%) and after breathing of filtered air for 18 to 20 hours (227.6%). During the smoggy period the figure for residual air was slightly lower in eight cases, there was no significant change in three, and there was a slight increase in two cases (fig. 1*C*; table 2). In 10 of the subjects there was a slight decrease in the residual percentage of total lung capacity and in 3 a slight increase on breathing of filtered air (fig. 1*D*). The average percentage of total lung capacity after breathing of the smoggy air was 50.3% and after breathing of filtered air for 18 to 20 hours 47.3%. The measurements obtained during the clear air period revealed no significant change, except for one case in which there was an increase. The average percentage of residual air for the seven subjects for the nonsmoggy period was 224.8% as compared to 227.6% after breathing of the filtered air for 18 to 20 hours. The average residual percentage of total lung capacity after breathing of the clear air was 57.4% and after breathing of filtered air for 18 to 20 hours 58.4%, or no significant change (fig. 1*D*).

The measurements of total vital capacity, the timed vital capacity for three seconds, the maximal breathing capacity, the alveolar nitrogen concentration after seven minutes of breathing oxygen, and the ventilation factor showed no significant average change during either smoggy or nonsmoggy periods after subjects had been exposed to the filtered air for 18 to 20 hours (table 2). The decrease noted in the volume of residual air, although of small magnitude after 18 to 20 hours of exposure to filtered air during smoggy periods, was significantly different from the results obtained after short exposure (two to four hours) to filtered air. There was no significant change in the lung volume measurements in the group of subjects studied during nonsmoggy periods after they had breathed filtered air for 18 to 20 hours.

In 22 subjects the percentage of residual air was compared during smoggy periods and after breathing of filtered air for 40 to 90 hours, with an average time of 55 hours (fig. 2*A*). The absolute volume of the residual air was decreased in all 22 after prolonged breathing of filtered air (173.9%) as compared to breathing of Los Angeles smoggy-air (203.4%) (table 2; fig. 2*A*). Volume of residual air as a percentage of total lung capacity was decreased in 21 subjects, with no change in one when breathing filtered air for 40 to 90 hours (43.4% for filtered as compared to 48.6% for smoggy air [fig. 2*B*]). The average percentage of residual air in three subjects breathing clear Los Angeles air was 184.7%, and it was 188.3% after breathing of filtered air for 40 to 66 hours. The residual percentage of total lung capacity was 41.7% for the nonsmoggy period as compared to 43.2% after breathing of the filtered air, or no significant change (table 2).

In 14 subjects there was a slight increase in the maximal breathing capacity after breathing of filtered air for 40 to 90 hours, in 7 no significant change, and in one a slight decrease (fig. 2C). The average of the maximal breathing capacity as a percentage of normal predicted for the 22 cases after breathing the smoggy air was 47.9, as compared to 51.7% after breathing of filtered air.

Bronchospasm was present in all cases. The maximal breathing capacity as a percentage of normal predicted was increased by one bronchodilator treatment from 1 to 30.0% (average 9.8% before and 7.8% after breathing of the filtered air).

In 13 subjects there was a slight increase in the timed vital capacity for three seconds after breathing of the filtered air, and in 9 there was no significant change. The average of the timed vital capacity for three seconds while subjects breathed the Los Angeles smoggy air was 55.5%, as compared to 60.3% after breathing of the filtered air. The ventilation factor was increased from 54.1% on breathing of smoggy air to 59.6% with filtered air. There was no significant change in the timed vital capacity for three seconds, the maximal breathing capacity, or the ventilation factor in the three subjects studied during nonsmoggy periods and after breathing of filtered air (table 2).

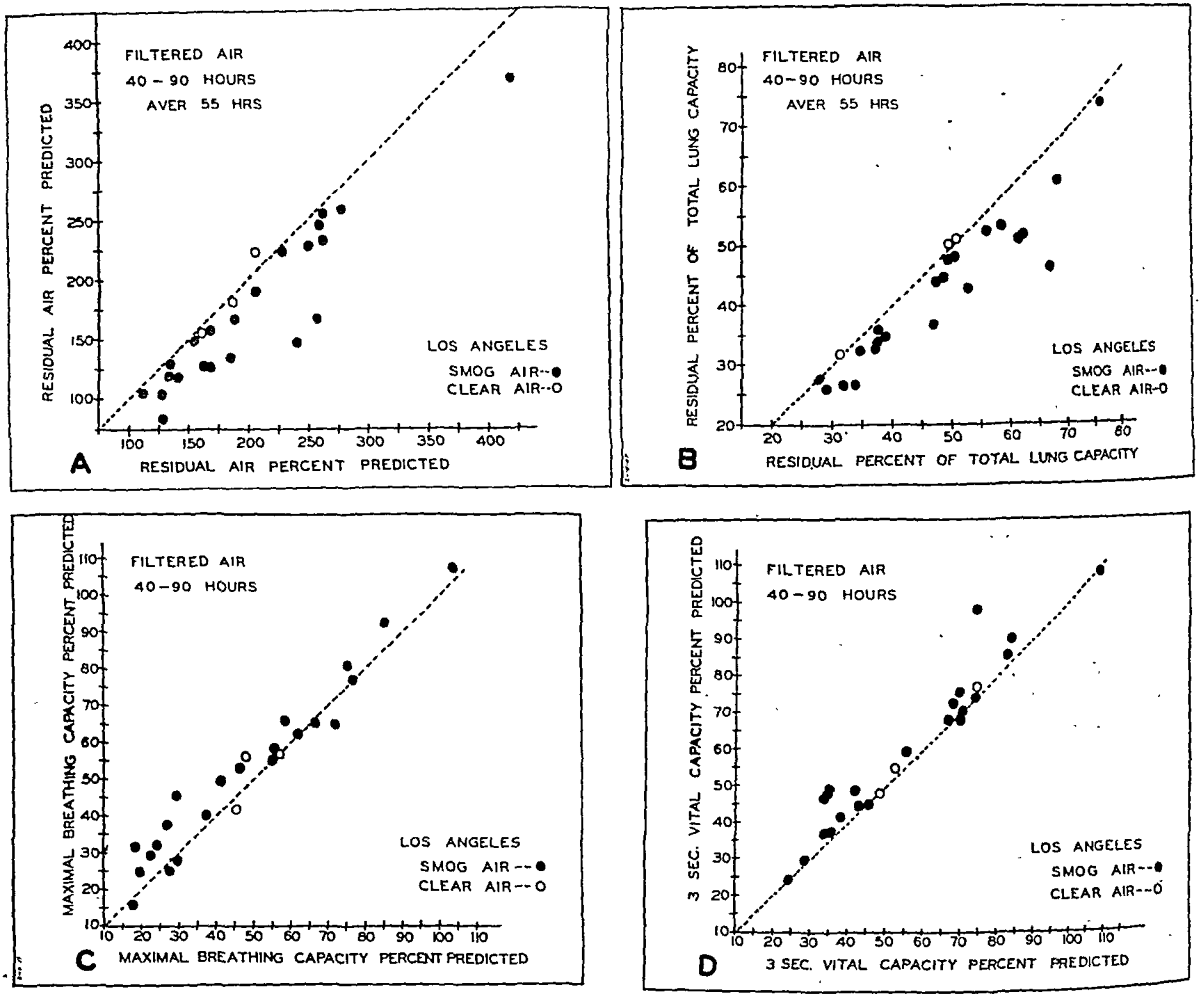

Fig. 2.—Comparison of effect of breathing filtered air with that of breathing smoggy air in 22 cases and clear Los Angeles air in 3 cases. Percentage of residual air (*A*) and percentage of total lung capacity (*B*) are plotted as in figure 1. Maximal breathing capacities as percentage of normal predicted (*C*) are plotted as abscissae for subjects who breathed smoggy air and as ordinates for those who breathed filtered air. Timed vital capacity for three seconds as percentage of normal predicted (*D*) is compared as with maximal breathing capacity data from *C*.

The nitrogen washout time was studied with the nitrogen meter in 14 subjects breathing smoggy air and after breathing of filtered air for 40 hours or more (fig. 3). In group A (average of five subjects) the end tidal nitrogen concentration was 1% after six minutes of breathing oxygen, an essentially normal nitrogen washout time and indication of uniform air distribution in the lung. There was no improvement in the nitrogen washout in group A after breathing of filtered air (average washout time, 49 hours). In group B the nitrogen washout was moderately prolonged, and an improvement was noted in four subjects after breathing of filtered air (average, 54 hours). In group C (average of five subjects) the nitrogen washout was markedly prolonged, indicating extensive disturbance in the uniformity of air distribution in the lung. The nitrogen washout was significantly improved after breathing of filtered air (average, 53 hours), indicating improvement in the uniformity of air distribution in the lung (fig. 3). The alveolar nitrogen concentration was slightly lower with breathing of filtered air as compared to smoggy air (table 2).

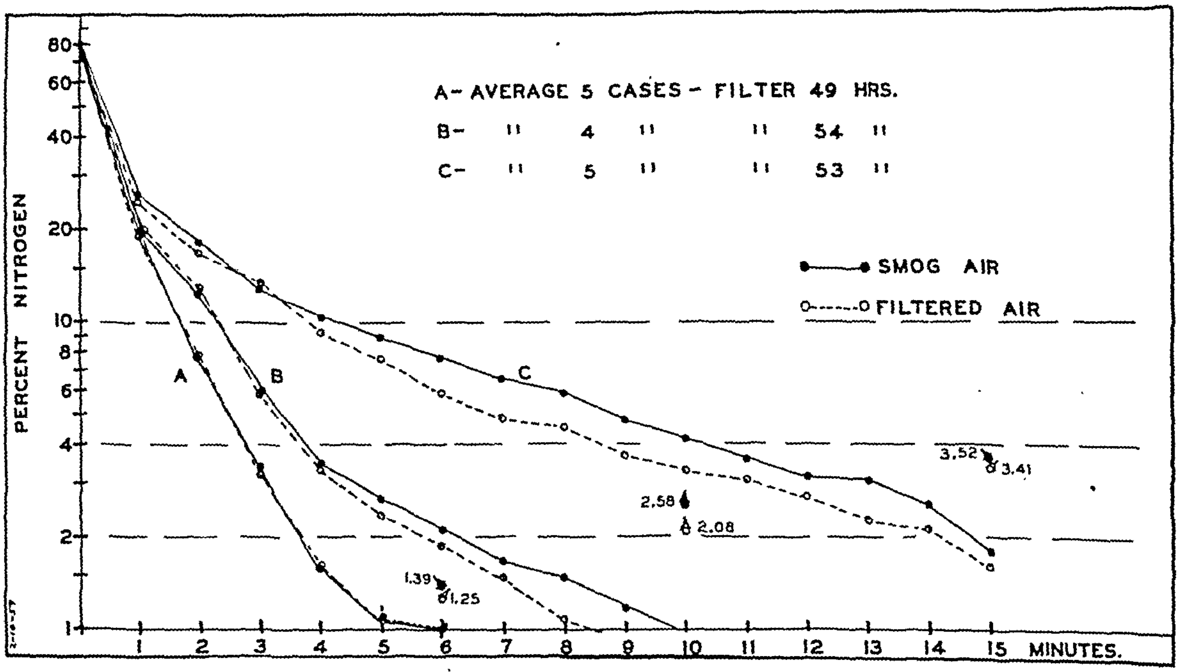

Fig. 3.—Comparison of rates of nitrogen washout in persons breathing oxygen. Data were obtained by means of nitrogen meter and continuous recordings of each breath for 14 subjects who had breathed filtered air 40 hours or longer. Percentages of nitrogen in expired air are plotted as ordinates with semilog paper and time of oxygen breathing as abscissae. In group A there was essentially normal nitrogen washout time to end tidal nitrogen concentration of 1% after six minutes of breathing oxygen; in group B, moderately prolonged nitrogen washout time; and in group C, marked prolongation of nitrogen washout on breathing of smoggy air. Average alveolar nitrogen concentration at end of washout is shown for each group.

Comment

In these studies, during smoggy periods in the Los Angeles area a significant improvement in lung volume could be measured quantitatively in subjects with emphysema after breathing of filtered air for 40 hours or longer. No significant changes were observed in volunteers without significant emphysema studied in a similar manner. An adequate number of studies has not been obtained to permit a comparison of blood-gas exchange measurements during smoggy periods, but preliminary data indicate that such changes are not as marked as those in lung volume. Studies have been obtained on pulmonary compliance in a few cases with a method previously described,[13] but more data are needed for evaluation.

Measurements of the carbon monoxide-diffusing capacity of the lung, by means of the steady state method of Filley and co-workers,[14] were obtained on five subjects before and after their residence in the filtered-air room for 44 to 64 hours (average, 48 hours). Although the number of studies performed was too small to allow evaluation, no significant difference was observed in carbon monoxide-diffusing capacity after breathing of filtered air, whereas there was a significant decrease in the residual air measurement. Carey[15] has reported impairment of diffusion capacity as a result of air pollution in Cincinnati.

The most significant improvement in lung volume measurements with breathing of filtered air was the decrease in the volume of residual air in the subjects with emphysema. The residual air measurement in persons with chronic pulmonary disease has a very wide spread with respect to the normal predicted value, one greater than that of any of the other tests of lung function used. In patients with emphysema the volume of residual air may be increased by bronchospasm, which frequently occurs during episodes of infection with retained secretions. Edema of the bronchial wall produces narrowing of the lumen, similar to bronchoconstriction, also impairing the uniformity of air distribution in the lungs. Breathing of Los Angeles polluted air appears to induce similar changes in patients with severe chronic pulmonary disease. Exposure lasting two or more days is probably required to attain the maximal effect. A similar delayed effect before the previous condition was restored was noted after the smog was removed. The data in this study indicate that when the subjects breathed filtered air for less than 40 hours, such as 18 to 20 hours, the improvement was very much less, with only slight decreases in the volume of residual air and no significant change in the timed vital capacity for three seconds or the maximal breathing capacity.

No improvement was noted after breathing of filtered air for two to four hours, and the average measurements in these studies showed even poorer results. The increased impairment of lung volume after the breathing of filtered air for two to four hours probably represents the effect of fatigue on the subjects, since all of the measurements were performed on the same day. The numerous measurements required to complete the study, with the close check of the volume of residual air, were very fatiguing for many of the subjects, especially those with severe emphysema. This factor was removed during the medium-to-long-exposure tests in the filtered-air room. The studies were done on separate days and every attempt was made to minimize the effects of fatigue. This meant the elimination of some tests that would have been desirable for this study but were objectionable to some subjects (such as arterial puncture) and use of the tests previously discussed which could be performed on all the volunteers with minimal discomfort and which appeared to be most apt to detect slight changes.

The moderate duration (18 to 20 hours) in the filtered-air room produced a slight improvement in the subjects with emphysema but no significant change in the group without this condition. The decrease noted in the volume of residual air after breathing of filtered air for 18 to 20 hours during smoggy periods, although of small magnitude, was different from the result obtained after the short exposure (2 to 4 hours) to filtered air. The subjects studied during nonsmoggy periods had no significant change in lung volume measurements after breathing of filtered air for 18 to 20 hours.

The data on the 22 subjects studied during smoggy periods before and after breathing of filtered air for 40 hours or more are impressive because of the reduction noted in the volume of residual air in all cases and of the significance of this reduction in terms of physiological changes in the lungs. There was also a significant improvement in the timed vital capacity for three seconds and the maximal breathing capacity, although the magnitude of these changes was not as great nor as consistent as was that in the residual air measurement. In three subjects studied initially during nonsmoggy periods and then placed in the filtered-air room for 40 hours or more there were no significant changes in the measurements obtained.

Improvement in the uniformity of air distribution in the lung on breathing of filtered air (as demonstrated by the nitrogen washout curve) was most marked in the patients with severe emphysema, less marked in those with a moderate degree of emphysema, and lacking in the absence of significant emphysema (fig. 3). Bronchospasm, edema of the bronchial wall, and retention of mucus and secretions, occurring in the presence of infection superimposed on emphysema, increases the nonuniformity of air distribution in the lung.

It would appear most likely that the improvement noted on breathing of filtered air results from the removal of substances in smog which irritate the bronchial mucosa. A long period of time was required to obtain the maximal reversal of the changes resulting from prolonged breathing of smoggy air (40 hours or more). It does not appear that the longer periods of filtered-air breathing (up to 90 hours) were significantly more effective than 40 to 50 hours, but the 40-hour interval was significantly better than the 18-to-20-hour interval. Kotin and Falk[6] have demonstrated that smog affects the ciliary movement of the bronchial mucosa, and this could be a factor favoring the retention of secretions during smoggy periods. After staying in the filtered-air room for two to three days, some of the subjects with severe emphysema had a marked increase in the amount of secretions raised. Removal of the irritating effects of smog, with an improvement in the ciliary action of the bronchial mucosa, could represent a significant factor in promoting the bronchial drainage noted clinically.

These studies indicate that the impairment produced by breathing smog aggravates the pulmonary insufficiency already present in chronic pulmonary disease. This response may be reversed by removing the smog from the air breathed, but there is a delay in the disappearance of such adverse effects. These data also indicate a lag in the onset of the maximal effect from breathing of smoggy air, so that a delay of two days or more could be expected before the maximal adverse effects were produced by the concentrations of the pollutants that now exist in the Los Angeles basin. Delayed response has been observed clinically during acute episodes of air pollution such as occurred in the Meuse Valley in Belgium, in Donora, Pa., and in London.

The health aspects of air pollution were regarded of sufficient importance in 1955 by the 84th Congress to merit scientific study and passage of Public Law 159, which established the air pollution medical program of the division of special health services, Department of Health, Education, and Welfare. This agency was instructed to determine whether or not and in what ways air pollution modified health among human populations.[16] That smog constitutes an important health problem in Los Angeles was indicated by the resolution proposed by the smog committee and adopted on Dec. 8, 1958, by the council of the Los Angeles County Medical Association, as follows: "The Smog Committee of Los Angeles County Medical Association reiterates that air pollution represents a present deleterious influence on the public health, as well as an imminent danger of catastrophic proportions. There are many different air pollutants which are injurious to health. Every opportunity should be taken to diminish them. Sulfur dioxide is one of the harmful components of air pollution which must be controlled."

The reaction of the air pollutants with other substances may increase their toxicity as combined smog and fog. Amdur [17] has shown that an aerosol of sodium chloride markedly increases the acute effects of low concentrations of sulfur dioxide on airway resistance in the guinea pig. Sulfur dioxide concentrations in Los Angeles air are highest at night and at a time when fog is more prevalent.

Activated carbon filters have been recommended for use both at home and in the office by patients with severe emphysema residing in smoggy areas. Some new buildings erected in Los Angeles have air conditioning combined with air filtration over activated carbon to remove smog. Portable activated carbon filters are being used at the Hospital of the Good Samaritan during periods of severe smog as a part of the treatment regimen for some patients with advanced pulmonary emphysema. The use of the carbon filter has been observed clinically to be of significant value in treating the patient with severe emphysema who suffers superimposed infection and bronchial obstruction in the presence of smog. The adverse effect of smog as demonstrated in this study provides a rational basis for the use of carbon filters and justifies their expense.

Conclusions

Significant objective quantitative improvement in the ventilatory characteristics of persons with severe pulmonary emphysema occurred after filtered air was supplied to replace the smoggy air of Los Angeles. The severity of the emphysema was aggravated by smog, but this effect could be reversed by breathing of filtered air for 40 hours or more, which demonstrated a delay in the disappearance of the effect. Measurement of residual air was the most sensitive test used in this study, and an increase in this measurement represents an early effect of smog. No significant changes in lung volume measurements were demonstrated from the breathing of filtered air as compared to smoggy air by the essentially normal person.

The use of activated carbon filters both at home and in the office has been recommended for patients with severe emphysema residing in smoggy areas. These studies suggest that the Los Angeles smog could present a serious problem for the person with chronic respiratory disease during prolonged periods of adverse weather conditions with high concentrations of air pollutants.

1212 Shatto St. (17) (Dr. Motley).

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PROBLEMS ASSOCIATED WITH ASPIRATION OF GRASS HEADS (INFLORESCENCES)

Anthony P. Clery, M.B., B.Ch., F. Henry Ellis Jr., M.D.
and
Herbert W. Schmidt, M.D., Rochester, Minn.

Grass heads, such as the inflorescences of timothy and barley, have on occasion been aspirated into the lungs, especially by children. Fourteen new cases are here added to 51 described by previous authors. The foreign body usually descends into the right bronchus rather than the left. The inflorescence of timothy is classed as nonextrusive; it generally remains in the bronchus until removed by bronchoscopy or pulmonary resection. Inflorescences like those of barley are classed as extrusive because they are so barbed that respiratory movements may carry them through lung tissue and pleura until they finally reach the outside through a sinus. Early symptoms after the aspiration are severe and alarming; pneumonitis invariably appears, often within 24 hours. On the basis of their own experience the authors recommend immediate bronchoscopy. If it fails they advise performing early thoracotomy rather than waiting for spontaneous extrusion.

Aspiration of a foreign body is not uncommon and management of the resulting syndrome is standardized. However, it is less well known that the inflorescence, or flower-bearing part, of a grass may be inhaled and may cause characteristic pulmonary disease. The purpose of this paper is to bring this little-known clinical syndrome to the attention of physicians and to emphasize certain points in its diagnosis and management.

The first reported case was that of a young French nobleman, Armand de Bautrée, who, it was reported in 1662, had carelessly put an ear of barley in his mouth. It adhered to his palate and he was unable to extract it. The ear was aspirated. He endured "a violent fever accompanied by a great difficulty in breathing, a dry cough, afterward spitting of blood, sleeplessness, and a great pain in his right side. A tumor at length appeared on that side and a surgeon extracted from it an ear of barley. . . ."[1]

Jackson's[2] paper of 1952 dealing with 35 cases of grass-head aspiration, including 7 from his personal files, is a classic in this field; in it is to be found the bulk of the basic knowledge on this subject. In our review of the literature we have found 16 more cases[3] and a search of the Mayo Clinic files revealed another 14. Information on these 65 patients forms the basis of this paper.

Botanical Considerations

The plant family Gramineae (grasses) is characterized by a typical head, or inflorescence, the unit of which is the spikelet (fig. 1). These are arranged in rows and project upward at an angle from the rachis, or central axis, of the inflorescence. A spikelet is a group of one to five sessile flowers borne on a short axis or rachilla. At the base of the spikelet, enclosing the flower or flowers, are two bracts, called glumes. These are the lower glumes. Two other bracts, the flowering glume and the palea, are immediately adjacent to each flower. The glumes can be of various shapes, for example blunt, sharp, or boat-shaped. Some have a needle-like projection, or awn, which may be attached to its tip (terminal awn) or to its back (dorsal awn). The spikelets of the inflorescence may be either loosely arranged, as in the genus Avena (oat), or tightly packed, as in Phleum pratense (timothy). The inflorescences of many grasses are often referred to as spikes.[4]

Among the 65 cases accurate classification of the grass head or inflorescence was a rarity. In 13 instances such nonspecific terms as grass spike, cereal spike, head of grain, head of grass, and ear of grain were used to describe the particle.[5] Most frequently only a common name was used, such as barley, wild barley, oat, wild oat, wild wheat, rye, millet, rice, foxtail, and cattail.

However, in some cases the inhaled inflorescence was accurately classified (table 1).[6] In 17 instances timothy grass inflorescences were apparently inhaled. The timothy grass, Phleum pratense, is widely cultivated in the pastures of the well-watered northeastern sector and northwestern coastal areas of the United States[7] as well as in Europe and the temperate parts of Asia and of the Southern Hemisphere (fig. 2).[4] It is interesting that its aspiration has been reported only from North America. Jackson[2] identified Phleum pratense in

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seven cases. Woolley[30c] published reports of two instances of the aspiration of an inflorescence of the "common timothy grass." The inflorescence in eight of our patients was recorded as a timothy head and this probably was indeed Phleum pratense (cases 1 to 8). In two cases in which the specimen was available we identified it as such (cases 5 and 7).

Many instances of aspiration of an inflorescence of the barley grasses (Hordeum) have been reported. This genus is indigenous to the temperate zones of both hemispheres, and in the United States flourishes in the dryer grasslands of the southwest.[4] One variety, Hordeum murinum, wall barley, is well known to cattlemen (fig. 2). Its inflorescence can penetrate crevices in the mouths of animals and has killed horses and cattle by perforating their intestines.[8] It was responsible for the illness of one of Godfrey's[30b] patients. Windsor[30] reported a case in which a spike of Hordeum leporinum was inhaled, and in one of our patients the spike was that of Hordeum, probably murinum (case 14). Including these three instances, and also one of our cases (case 12) in which the barley was not classified, aspiration of a barley spike has been recorded 14 times.[9] We believe this number would be greater if accurate classification of the inflorescence were available in more of the 65 cases.

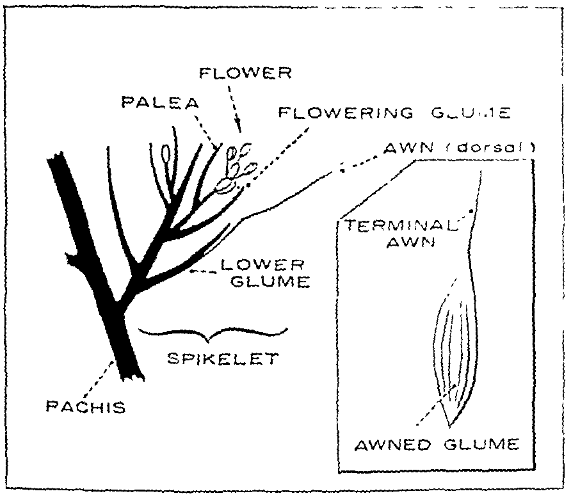


Fig. 1.—Diagrammatic representation of parts of inflorescence or grass head. Inflorescence contains many spikelets which project at angle from rachis or central axis. Lower glumes, flowering glume, and palea all form chaff. Awn is whisker-like projection from dorsum or apex (*inset*) of glume.

The next most frequently inhaled grass heads belong to the genus Avena or Trisetum, the oats, and their aspiration has been reported in five cases. Accurate classification was available in two; these were Avena fatua and Trisetum flavescens.[10] Because of the loose nature of the inflorescence it is likely that merely a spikelet was inhaled in most of these. In one of the reported instances the foreign body was called "an oat,"[2] while in a case of ours it was described, by the person who performed bronchoscopy, as a "hull of oat with four spicules attached" (case 13). This genus has fairly typical inflorescences, and it seems reasonable to assume that these five cases are probably accurately classified.

TABLE 1.—*Types of Grass Heads (Inflorescences) Accidentally Aspirated*

Common Name	Classification
Timothy	Phleum pratense
Barley	Hordeum
Oat	Avena (syn. Trisetum)
Rye	Secale
Foxtail	Alopecurus
Sandbur	Cenchrus
Wheat	Triticum
Brome	Bromus

The inflorescences of the rye and the foxtail genera, Secale and Alopecurus, have also been aspirated a number of times.[11] It would seem to us that they could easily be mistaken, by the inexpert, with each other and with those of Hordeum, Triticum, and Bromus (barley, wheat, and brome grasses). Borrie's[31] patient aspirated an inflorescence of the brome grass, Bromus catharticus, and died. Two of our patients inhaled inflorescences that in the operative note were called sandburs. Since these are so typical in appearance we feel that, indeed, they probably belong to the genus Cenchrus (cases 9 and 10).

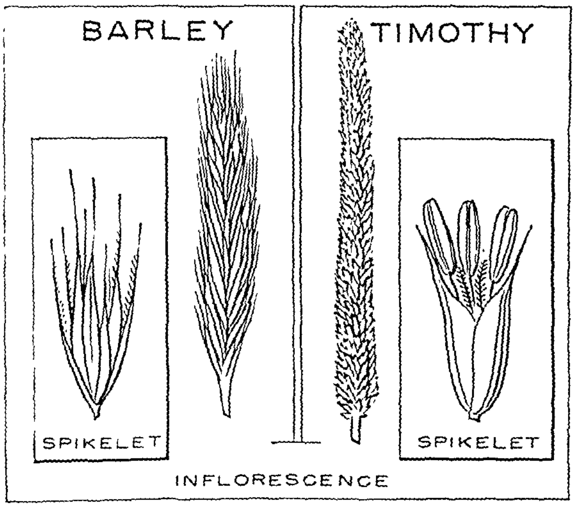


Fig. 2.—Inflorescences of timothy (Phleum pratense) and wall barley (Hordeum murinum). Insets represent their respective spikelets (enlarged). Glumes and awns projecting at angle from inflorescence prevent its expectoration, and, those of barley being stiffer and more resilient, may allow it to be driven through lung and chest wall.

Pathology

When an inflorescence is aspirated it always enters the respiratory passages with the stump of the rachis (or rachilla in the case of a spikelet) leading and with the glumes and the awns, if present, trailing. This has bearing on its subsequent behavior.

Clinically there are two types of inflorescence: One remains in a bronchus unless removed at endoscopy, while the other is forced, by respiratory movements, toward the periphery of the lung and sometimes even through the chest wall.[12] We refer to the first type as nonextrusive and to the second type as extrusive. The inflorescences of different genera of grasses have varying characteristics and these, to a large extent, determine the type.

The spikelets of the genus Phleum, to which timothy grass (Phleum pratense) belongs, lie flat against the rachis and are small and crowded, forming a cylindrical inflorescence. The glumes of timothy, about 2 mm. in length, are thin and membranous, lack an awn, and become soft when moistened on inhalation (fig. 2). There is some tendency for an inflorescence of this species to migrate down the bronchus, but this tendency is not great enough to drive it through the lung. Timothy is of the nonextrusive type.[13]

TABLE 2.—*Data on Fourteen Mayo Clinic Patients Who Aspirated Grass Heads*

Case	Sex	Age First Seen, Yr.	Month Inhaled	Inflorescence	Site*	Length of Lodgment	Treatment	Results
1	M	1 3/12	June	Timothy, 1.0 x 0.4 cm.	L.M.B. & L.L.L.	3 day (?)	Bronchoscopy	Recovery; accidental death 14 yr. later
2	M	8	June	Timothy	R.L.L.	26 mo.	Bronchoscopy	Residual bronchiectasis, lobectomy 10 yr. later, eventual recovery
3	M	20	June	Timothy, 5.5 x 0.5 cm.	R.L.L.	7 day	Bronchoscopy	Recovery
4	M	1 2/12	August	Timothy	R.M.B.	1 day	Bronchoscopy	Recovery
5	M	5 6/12	October	Timothy, 2.5 x 0.5 cm.	R.L.L.	9 mo.	Segmentectomy	Recovery
6	M	2 9/12	July	Timothy, 1 in. long	R.L.L.	20 hr.	Bronchoscopy	Recovery
7	M	3 8/12	June	Timothy, 4 x 1 cm.	R.L.L.	34 mo.	Lobectomy	Recovery
8	M	1 3/12	June	Timothy	L.M.B.	10 hr.	Bronchoscopy	Recovery
9	F	2 6/12	May	Sandbur	R.L.L.	22 mo.	Bronchoscopy	Recovery
10	F	1 3/12	August	Sandbur	R.M.B.	5 mo.	Bronchoscopy	Recovery
11	M	18	October	Cattail (?)	R.L.L.	8 yr.	Lobectomy	Recovery
12	M	5	September	Barley (?)	L.L.L.	14 mo.	Bronchoscopy	Recovery
13	F	8/12	July	Oat (spikelet?)	R.M.B.	1 day	Bronchoscopy	Recovery
14	F	11 8/12	Unknown	Hordeum (murinum ?) (barley)	R.L.L.	9 yr.	Lobectomy	Recovery

* L.M.B. = left main bronchus; L.L.L. = left lower lobe; R.L.L. = right lower lobe; R.M.B. = right main bronchus.

The spikelets of barley grass, on the other hand, are set at an acute angle to the central rachis of the inflorescence, their glumes and awns are stiff and resilient, especially in autumn, and they are not affected by moisture. Therefore, they act like the barbs of a fishhook and prevent extraction of the grass head (fig. 2). Inflammation and liquefaction in front of the spike often allow its progression through the lung and chest wall, and it reaches the outside through a sinus.[3] Woolley [3g] has noted that if it is aspirated during early summer, while soft and immature, the spike does not perforate the chest wall.

The inflorescences of most of the other grass genera behave like barley and are grouped into the extrusive type. However, in the two cases in which a sandbur was inhaled the bronchoscopist was able to extract it. In both it had lodged in a large bronchus, namely, the right lower-lobe bronchus and the right main bronchus respectively (cases 9 and 10). We have classified sandburs as belonging to the nonextrusive type and postulate that the short stiff spines projecting in all directions from these small, roughly spherical inflorescences prevented their being forced deeply into the lung.

Incidence

As is usual with aspirated foreign bodies, the majority of patients are young children, although adults and adolescents are not immune. In only 14 of 55 cases in which the age was recorded was the patient more than 10 years old. The sex was recorded in 50 patients—31 males and 19 females. Since grasses flower in the warmer months, it is obvious that most patients become afflicted in either summer or autumn. The month of aspiration, recorded in 13 of our cases, fell between the first of May and the end of October in every instance.

Symptomatology

In many of the reports detailed clinical data are lacking, and we have found that anything approaching a full statistical analysis is impossible. The following discussion of symptomatology, therefore, will be conducted in a general manner (table 2).

Diligent questioning frequently elicited a history of the accident. The child may have been seen playing with or "smoking" a grass head. Sometimes it is thought to have been inhaled or swallowed. Six of our patients (cases 1, 3, 4, 6, 8, and 13) came to the clinic within a week of their accident. Five gave a history of aspirating a grass particle and one was sent by a physician who suspected a foreign body. Our remaining eight patients had retained their inflorescences for periods ranging from five months to nine years; five of these (cases 2, 5, 10, 11, and 12) gave a history of inhaling or "swallowing" a foreign body which, in three, was known to have been a grass head. One patient (case 9) had a sudden onset of respiratory symptoms, but aspiration of a foreign body does not seem to have been considered. In the other two patients (cases 7 and 14) there was neither a history of aspirating a foreign body nor a history of the onset of acute symptoms. All these eight patients had been under a physician's care many times and had been hospitalized once or more during their illness. Bronchoscopy had been performed on six of these patients before they came to us, but the diagnosis of an aspirated foreign body had not been made. Two of the eight patients had been treated for pulmonary tuberculosis, and one had spent 14 months in a sanatorium; tubercle bacilli were identified in neither case.

The initial symptoms, while common to inhalation of all foreign bodies, are frightening to the lay observer. There is sudden choking, coughing, and cyanosis, and gagging, retching, and vomiting are common. Jackson[2] has pointed out that an asthmatoid wheeze, although uncommonly noted by the lay observer, is an almost invariable initial symptom. This was a presenting symptom in three of our 14 patients (cases 4, 7, and 9); two of these, in whom the grass head had been present for many months, had continuous wheezing. After the startling initial stage a symptomless interval ensues. During it there may be an occasional cough or wheeze and the child may be apprehensive and sleepless (case 6).

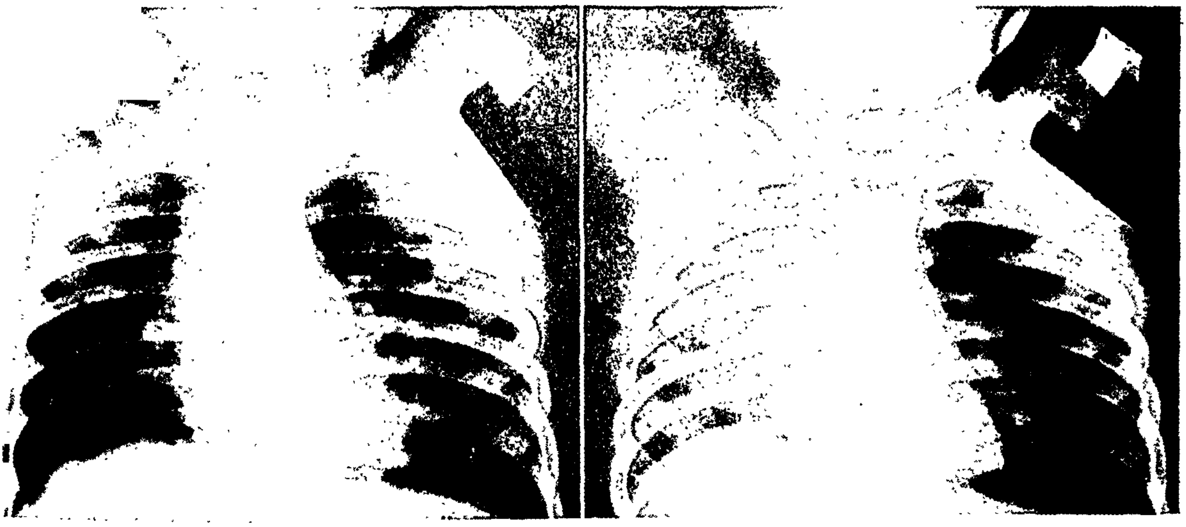


Fig. 3.—Roentgenograms from patient in case 8, showing obstructive emphysema of left lung. Timothy grass inflorescence that lodged in left main bronchus was removed 10 hours after its aspiration. Roentgenograms were taken during (*left*) inspiration and (*right*) expiration.

Invariably pneumonitis develops quickly, often within 24 hours, and with it rapid pulse, fever, and labored respiration. It is usually thought to be simple pneumonia. Paroxysms of coughing may continue, with attacks of choking and cyanosis. In time the cough becomes productive and the sputum purulent and often blood-streaked. Later there is frankly foul expectoration and the breath is fetid. All the stigmata of chronic pulmonary disease are apparent: The temperature is elevated, there are drowning sweats and chills, the child becomes wizened and fails to gain, and thoracic osteoarthropathy may be noticed.

Hemoptysis is common. It is usually recurrent and may even occur daily. Massive hemorrhage may occur,[14] but small amounts of blood are the rule. Eight of our patients reached the chronic stage; hemoptysis was recorded in five. Before coming to the clinic one (case 12) had coughed up blood so many times that he needed several blood transfusions. Another patient (case 14) had a severe hemoptysis, amounting on one occasion to a pint. One of the physicians who saw this patient before she came to us suspected a vascular tumor. Anemia would be expected, but in our eight patients who reached this chronic stage the concentration of hemoglobin was not significantly depressed.

Although pain has not been frequently mentioned, either in our cases or in the previously published cases, it must be a feature in many. It can be due to pleurisy over the inflammatory process in the underlying lung and it must be excruciating when a grass head burrows through the chest wall.[1] A foreign body in the right lower lobe can cause right-sided abdominal pain and even muscle rigidity. This had led to appendectomy in four patients; all the appendixes were normal and their removal gave no relief.[15] Spontaneous expectoration of a timothy head has not been reported, but in three cases an extrusive inflorescence has been coughed up.[14] In all, massive hemorrhage was a feature. One patient needed emergency lobectomy under heroic conditions for its arrest.[3b] Verrotti[3c] made the interesting observation that the grass head, in his case, was expectorated in the center of a large clot.

Physical Signs.—The physical signs are usually found over the base of the right lung. The right bronchus is more vertical than the left and is therefore the usual lodging site of a foreign body. The side in which the inflorescence had lodged is recorded in 42 of the 65 cases; it was the right in 38.

Referring to grass heads, Woolley[3c] has pointed out that ". . . lack of density [of an inflorescence] precludes either complete or ball-valve bronchial obstruction and development of massive atelectasis or emphysema." However, as Jackson[2] mentions, these processes do occur, although perhaps to a lesser degree than with some other foreign bodies. There is decreased expiratory excursion on the affected side. Resonance is diminished or increased, depending on whether there is collapse or obstructive emphysema. Breath sounds are diminished or absent.

The pneumonitis caused by an inflorescence is characterized by a large amount of inflammatory exudate which fills up the adjacent bronchioles and bronchi. Then breath sounds cannot be transmitted, so they are decreased or absent. In true pneumonia, tubular breathing would be heard.[2] In chronic cases there are signs of retained bronchial secretions and persistent pneumonitis in the base of the affected lung.

X-ray and Bronchoscopic Findings.—In the early stage thoracic roentgenograms show localized emphysema or collapse. In case 8 a roentgenogram taken 10 hours after the accident showed obstructive emphysema on the left (fig. 3). A head of timothy grass was removed from the left main bronchus. When pneumonitis ensues, the picture of consolidation will be superimposed on the underlying tendency to emphysema or atelectasis. In case 1 a roentgenogram taken about three days after the aspiration of a timothy head showed consolidation of the left upper lobe superimposed on lobar collapse (fig. 4). The grass inflorescence was found lying in the left main bronchus and obstructing the branch to the upper lobe. When chronic disease of the lung has developed, the x-ray findings are somewhat nonspecific. There is typically an area of persistent pneumonitis in the affected base, usually the right (fig. 5*a*). Bronchiectasis often seems the likely diagnosis. Bronchoscopy should be undertaken; if no foreign body is found, bronchograms should be made and these will usually confirm this impression.

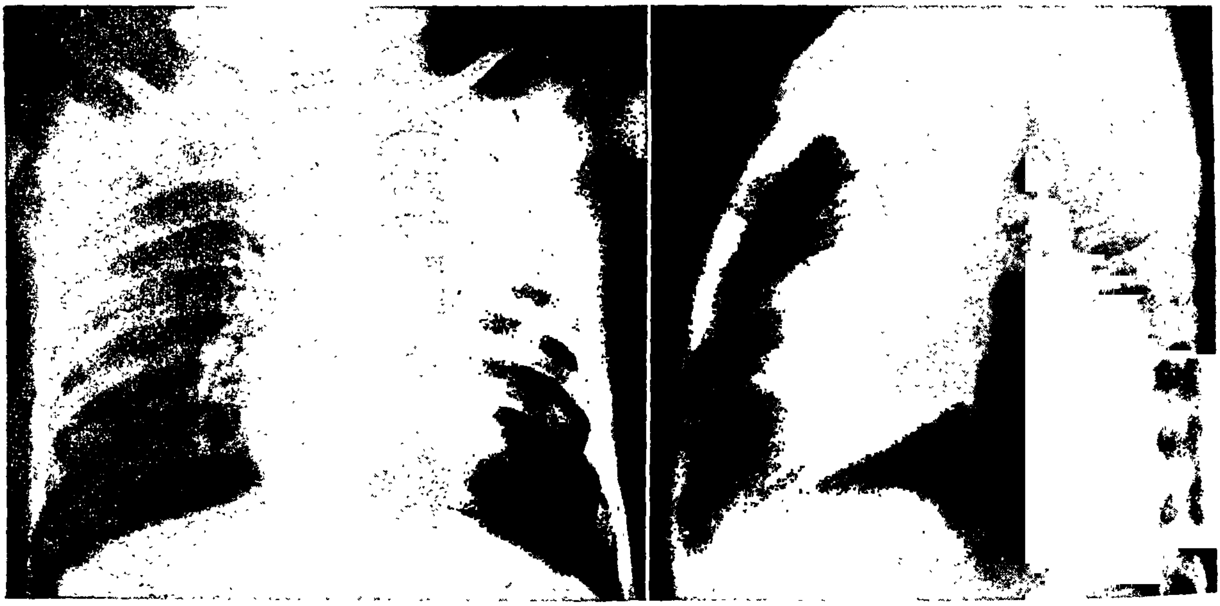


Fig. 4.—*Left*, posteroanterior and *right*, left lateral roentgenographic views from patient in case 1, demonstrating acute pneumonitis superimposed on collapse of left upper lobe. Inflorescence of timothy grass was removed from left main bronchus after stay of about three days. It had obstructed orifice to left upper-lobe bronchus.

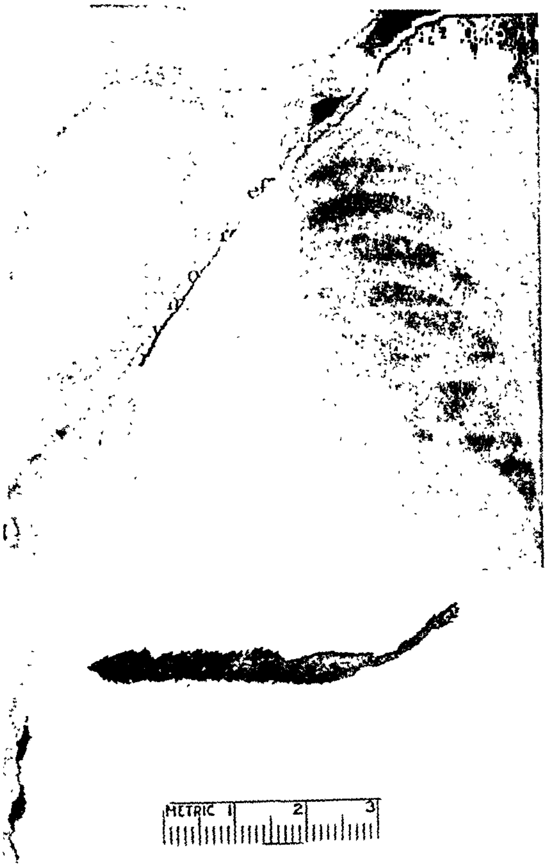
Treatment

When possible, endoscopic removal is performed. In the total of 19 cases of nonextrusive inflorescence there were 17 timothy heads and 2 sandburs (cases 9 and 10), and bronchoscopic removal was possible in 16. In three of the timothy-grass cases in which thoracotomy was necessary the grass head had been in the bronchus for 9, 10, and 18 months, respectively, while of the 14 patients who had aspirated timothy heads and on whom endoscopy was successful all but 2 retained the foreign body for shorter periods, namely, 9 months in one[2] and 26 months in the other (case 2) (fig. 5). The patient in case 2, it is interesting to observe, had a lobectomy done elsewhere 10 years later for residual bronchiectasis. It would seem that when a timothy inflorescence is present for more than nine months, resection is usually necessary. There were no deaths in patients who aspirated a nonextrusive type of inflorescence.

Of the 65 patients 46 probably inhaled an extru- e grass head. Of these, actual extrusion through e chest wall or the loin took place in 31 and spon- ieous expectoration in 3.[11] In only three was nchoscopy successful. Resection was necessary seven (fig. 6). Of these 46 patients 2 died.

Follow-up Observations.—The results of follow- examination were available on all our patients the time of preparing this report. Except for one ient who died accidentally, all were well and ie had any respiratory symptoms. Recent ic roentgenograms were available from four patients, two of whom (cases 3 and 10) had irated an inflorescence which was removed nchoscopically and two of whom (cases 7 and had originally required lobectomy. None demon- trated any disease of the lungs.

n the literature the information concerning late ilts is rarely detailed. Most patients have appar- ly recovered fully; however, bronchiectasis does m to be a rare sequela. Reference has been made ne such case, and Woolley [38] recorded two more which minimal bronchiectasis, largely asympto- tic, was found four and six years, respectively, ter bronchoscopic removal of the grass heads.



. 5.—*a*, roentgenogram of patient in case 2, showing nonitis in base of right lung. Similar findings were t in many cases. *b*, timothy grass head, aspirated 26 hs previously, was removed at bronchoscopy from right er-lobe bronchus of patient in case 2.

Two patients died as a direct result of inhaling a grass head, an extrusive type in each instance. A 12-year-old boy, reported on by Herbert Mayo in 1839 happened to have an ear of rye in his mouth while riding in a carriage. The carriage gave a jolt and the ear of rye disappeared. Later the patient died. Autopsy disclosed an abscess involving the liver and lungs. "On inspection, the ear of rye was found sticking, part in the liver, part in the lungs."[10]

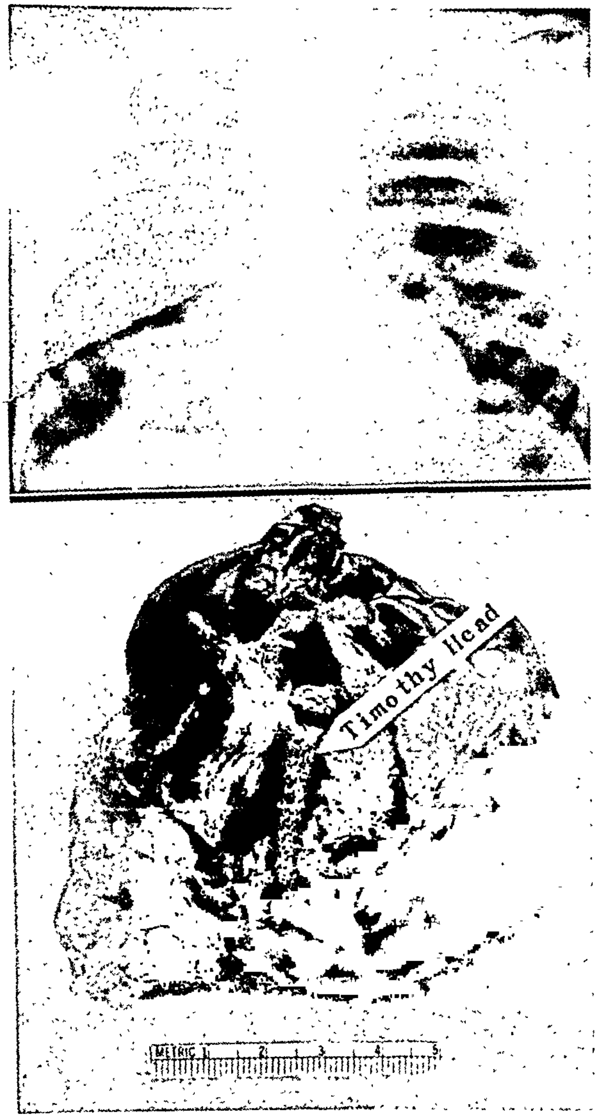


Fig. 6.—*Top*, roentgenogram of patient in case 7, showing pneumonitis in right lower lobe. It is similar to that in figure 5. *Bottom*, resected segment from right lower lobe. When it was sectioned, timothy head, surprisingly well preserved after having been inhaled 34 months previously, was found in bronchiectatic cavity.

Borrie [31] reported on a female infant, one year of age, who was admitted to the hospital in extremis. She appeared to have bronchopneumonia and was placed in an oxygen tent. Unfortunately, she died within two hours. At postmortem examination abscess of the lung, empyema, widespread collapse, and bronchopneumonia were found. A head of brome grass (Bromus catharticus) measuring 6 by 0.75 cm. was found in the pleural cavity.[17]

Comment

Despite the fact that many cases must have gone unreported, the aspiration of a grass inflorescence is obviously a rarity. However, it may lead to serious intrathoracic problems and we believe this diagnosis should be considered when a child is suspected of having inhaled a foreign body while out of doors during summer or autumn.

Prevention, as in most diseases, is the most effective means of combating the problem, and aspiration of any foreign body is frequently due to carelessness. As has often been pointed out, the mouth should not be used for holding inedible objects. When infants are put on the grass they should be placed on a large sheet or blanket, and children should not be allowed to play games in which grass heads are put in the mouth or "smoked."

Report of an early diagnosis has not been encountered in the literature. In reviewing the histories of our cases and those of others it is obvious, as Mahoney[3d] has pointed out, that frequently, even though a history of aspirating the foreign body is available, it is forgotten or ignored by parents and physicians alike. Minor respiratory ailments are usually diagnosed at the early stage. Other misdiagnoses include whooping cough, bronchopneumonia, asthma, diphtheria, pulmonary tuberculosis, chronic bronchitis, bronchiectasis, tubercular rib, vascular tumor, and acute appendicitis. It is obvious, on reviewing our cases and those in the literature, that the majority of these patients have been ill for many months and years because the true nature of their disease was never suspected.

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Brig. Gen. Floyd L. Wergeland (MC), U. S. Army

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On Dec. 1, 1958, I talked to the Clinical Session of the American Medical Association at Minneapolis. In the six months between that date and today, we have tabulated a tremendous amount of data on the Medicare program. Study of this material throws new light on the whole program and places our administrative problems in a new perspective. I will limit this presentation to one or two of the major points.

Service hospitals have, for a long time, provided care for dependents of men in uniform. However, they could not provide for all dependents. Some dependents, especially those separated from their sponsors, lived too far away to have access to a service hospital, or the hospital was not in a position to provide the care needed at the time

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The act provided that the spouses and children of uniformed personnel on active duty were to have the privilege of choosing freely between service hospitals and civilian physicians and hospitals. It further specified (sec. 201 C, public law 569, 84th Congress) that the right to such free election for dependents living with sponsors could be limited under regulations to be prescribed by the Secretary of Defense, after consultation with the Secretary of Health, Education, and Welfare, when adequate medical facilities for care were available in service hospitals.

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Growth and Reduction of the Program

The program grew with great speed; 90 days after it began, the total number of dependents of active duty personnel cared for increased to an annual rate of about 70% more than in the previous year, when care was available only in service hospitals. The total rate, for admissions in service hospitals and in civilian hospitals taken together, has increased very little since then. At the peak period, in the third quarter of the calendar year, 1958, the total program was only 7% larger than during the first quarter of its existence—an increase that hardly kept pace with the increase in the num-

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ber of dependents. In summary, the expanded program came into being, found a need, filled it almost immediately, and leveled off.

The expanded program, utilizing both service and civilian hospitals on a free-choice basis, filled an existing need by providing care for dependents who previously had to pay for care themselves. However, it also caused a shifting of a fairly substantial number of dependents who would normally have received care in service hospitals to civilian sources of care.

Part of this was desired because many service hospitals were overcrowded. But it went too far, and, in the spring of 1958 during the hearings on the appropriation for fiscal year 1959, the Congress recommended that the exception to the "free choice" principle embodied in the original Medicare act be enforced. Thus, service hospitals would be utilized to the optimum extent before dependents living with their sponsors were allowed to use civilian physicians and hospitals at government expense.

Since our service hospital systems must, to a considerable extent, be maintained on a ready-available basis in the event of hostilities, it is obviously a wise economic policy by Congress to see that such currently available facilities are used to provide care for dependents, up to the level of optimum operating efficiency. To achieve this goal is not an easy matter.

The over-all objective is in essence to preserve the identity and independence of service and civilian medical facilities but at the same time to coordinate them into a unified system which will provide effective, economical, uniform care to the spouses and children of men in the services, without adversely affecting either the military or the civilian practice of medicine.

Eligible Dependents

The statistical universe of dependents to be served by the Medicare program consisted of all dependent wives and children of active duty personnel. However, though the act was effective throughout the world, in practical terms it was largely limited in its civilian application to dependents living in the continental United States, Alaska, Hawaii, and Puerto Rico.

Our recently completed statistical studies showed that the 3 million dependents produce annually about 700,000 hospital cases. If permitted to exercise free choice, about 325,000 hospitalized dependents (about 45%) would use service hospitals and about 375,000 (about 55%) would use civilian facilities. Unfortunately, the distribution of cases shown here between service and civilian hospitals represents an underusage of facilities which must be maintained by service hospitals. Therefore, it was necessary to reverse these percentages, plus a little more which cannot be exactly determined in advance.

Developing procedures to reverse these percentages would have been difficult in itself. Unfortunately, as Rabelais' Gargantua puts it, we were at the same time "subject to a disease which at that time they called lack of money." Available funds simply would not cover the cost of our unrestricted free-choice program. This combination of problems created more than a routine predicament—it was a crisis.

Meeting the Money Crisis

The first step, and the one we were least willing to take, was to make certain that program costs for care in civilian facilities were reduced to a level that available funds permitted. This restriction applied to all dependents, whether living with or separated from their sponsors. The projected savings were, of course, a variable figure, dependent in part on another variable—the extent to which patients could be shunted to and cared for by service hospitals. This enigmatic lurking-in-the-background problem of service hospital capacity proved to be an insoluble one. Close study revealed that "optimum capacity" was a highly variable thing. As strength (and needs) of the armed forces change, as the intake of various types of cases fluctuates, as medical staffing changes, as seasonal fluctuations have their effect, as communicable diseases come and go, there will be corresponding changes in the significance of the term.

It was evident that the only general principle that could be applied on a priority basis was this: Dependents living with a sponsor and needing care would have to be required to seek it from service hospitals and could be allowed to use civilian facilities at government expense only if service hospitals were unable to provide the needed care. Dependents residing apart from sponsors, or on trips, would continue to have advantage of the free-choice principle for authorized care, merely by presentation of their identification card (DD form 1173) or other proper identification.

Decentralized Control of Permit System

Implicit in this principle was the fact that the only people who could determine the meaning and measurement of reasonable hospital capacity were the men on the spot who knew the hour-to-hour changing balance between needs and available facilities. Accordingly, that was the way the permit system was set up. The basic requirement and procedure is simple: "Living-with-sponsor" dependents are required to apply for needed care to a service hospital; if care cannot be provided, a permit will be issued which allows a dependent to receive care from civilian sources at government expense, if the needed care is authorized. This last phrase needs to be emphasized.

Since permits must often be issued by clerical personnel or by nonmedical officers commanding detached units without ready access to a service hospital, a permit is not a blanket authorization for care at government expense; it is a document which allows a dependent to seek civilian care, but only that care which is authorized may be billed under Medicare. The civilian physician consulted is the one who determines if the care required is authorized under existing regulations. In effect, this procedure is a device that comes as close as possible to guaranteeing optimum utilization of service hospitals. Basically, the permit system for those dependents who are living with a sponsor assigns primary responsibility for care to service hospitals, with civilian facilities handling the overflow.

Shifting Patterns of Care

The restrictions on types of care for which payment may be made, and the permit system, were adopted to reduce costs and to further insure optimum use of service hospitals. The universe of dependents, the over 3 million women and children to whom these regulations primarily apply, is not a static universe. Both "separated-from-sponsor" and "living-with-sponsor" groups have a constantly changing membership. For many reasons families do not remain either together or apart for predictable periods of time. For example, a man is transferred and his wife remains behind to hold a job, to have a baby, to see the children through school, or to take care of sick parents. Perhaps there is no housing at the new post, and then housing becomes available; or perhaps the husband is on sea duty or temporary duty. Then conditions change and family groups re-form or temporarily break up, and "separated-from-sponsor" dependents become "living-with-sponsor" dependents.

When we consider everything together—the changing universe of dependents with their changing locations and eligibility, the need to keep our costs down, and the need to keep service hospitals operating at optimum capacity—the complexities of the program begin to become apparent. It is in this kaleidoscopic context that we do our job.

May I call attention to the changes which present an almost insuperable obstacle to operating the Medicare program on conventional health insurance lines? From the vantage point of hindsight, we are now able to see that these facts fall into a pattern. At the time, the program appeared to be an unpatterned, or unpredictably patterned, process. Now, we are able to see the process for what it was—primarily a redistribution of maternity cases from service to civilian hospitals and their partial replacement in service hospitals by an influx of medical and surgical, mostly pediatric, cases. The most important reason for not seeing the over-all pattern earlier was the problem of the lag in billings. It is in this context of change that the program operates.

The Future

As to the future, we know that the restrictions on the program have reduced the total volume of care. What we do not yet know is the extent to which the service hospitals will be able to take over and do the job. We are watching the restrictions closely; as dependents, physicians, and hospitals learn to adapt to these changed conditions it may well be that we will eventually be able to restore some, perhaps all, of the care we have had to cut out of the program. Our goal is to give the maximum care that the law and our funds allow. It is our hope that events will work out so that the total amount of care given returns to a proper level. If we all work together, I think we can at least come close to reaching that goal. Eventually, we hope to stabilize the program by return of certain types of care previously authorized so that it will become a permanent feature of service life. If we do that, Medicare should prove to be one of the major foundation stones of that high morale which is the indispensable condition of freedom.

INTESTINAL MOTILITY AND THE FORMATION OF ADHESIONS.—With the use of a method of producing measured, similar trauma to the peritoneal surface of the small intestine in dogs, adhesions were formed after 14 days in 7 of 10 so treated. Filmy to medium strength adhesions involving one-third to two-thirds of the segment prevailed in the control group. When, in addition, intestinal contraction was stimulated by the administration of prostigmin, adhesions were observed in only 3 of the 11 so treated. Only one of these had adhesions of medium density and the segment in these 3 dogs was from one-third to two-thirds involved. When, however, atropine was administered in addition to the measured trauma, adhesions were observed in all 10 animals so treated. All but one of these dogs had adhesions of at least medium density and 7 of them had involvement of more than two-thirds of the segment. By inference, then, the use of drugs which inhibit peristaltic activity is undesirable following laparotomy, and paralytic ileus due to any cause may be presumed to enhance the persistence of intraperitoneal adhesions.—D. F. Cone, The Effect of Intestinal Motility on the Formation of Adhesions, *Bulleting of the Johns Hopkins Hospital*, July, 1959.

RADIOISOTOPIC STUDY OF EFFECTS OF IRRIGATING FLUID IN TRANSURETHRAL PROSTATECTOMY

Eldon M. Fillman, M.D., Otto L. Hanson, M.D.
and
Lael O. Gilbert, M.S., Topeka, Kan.

The amount of water that enters the blood stream as a result of irrigating the bladder during transurethral prostatectomy was determined in 11 patients. The extent of hemolysis was measured in nine and the volume of blood lost was measured in six patients. The determinations were made possible by measurements of radioactivity with Cr^{51} and I^{131} used as tracers. The average blood loss in two patients with cancer and four with benign hypertrophy was less than 280 cc. The water absorbed into the blood stream in 10 cases of benign hypertrophy averaged 237 cc.; in an 11th case the operation was unusually prolonged and the volume absorbed was 1,780 cc. The amount of hemolysis was equivalent to from 0 to 44 cc. of blood in eight cases in which distilled water was used as the irrigant; there was no hemolysis in the one case in which the irrigant was a solution isotonic with blood. Distilled water therefore appeared satisfactory as an irrigant under these conditions when the operation was not prolonged and the hydrostatic pressure was kept minimal.

Transurethral prostatectomy requires the use of an irrigating fluid to distend the prostatic urethra and to wash blood and dissected tissue away from the operative site. If bleeding is allowed to become active and profuse, a high head of pressure will be required to enable the operator to have adequate vision. Opened venous sinuses provide a channel for irrigating fluid to escape into the vascular system. For the most part the volume of fluid absorbed will depend on the hydrostatic pressure, the number and size of the venous sinuses opened, and the time of exposure.

It is recognized that the entrance of irrigating fluid into the vascular system has, in the main, two adverse reactions. If sterile water is used as the irrigant, hemolysis will result.[1] If a large volume of irrigating fluid enters the vascular compartment, cardiac decompensation may occur.

Hemolysis can be avoided by the addition of a substance such as glycine to water to render it iso-osmotic and nonhemolytic. The role of hemolysis in the pathological physiology of acute tubular necrosis is unknown. Creevy [2] feels that hemoglobinemia of high concentration bears a direct relationship to the development of acute tubular necrosis. It is recognized that other important factors are shock, hypotension, hemorrhage, bacteremia, preexisting kidney damage, extravasation, and excessive fulguration.[3] Creevy [4] reports that the use of an iso-osmotic irrigating solution has reduced the mortality of transurethral resection from 1.29 to 0.6%.

The danger of overhydration has been recognized in recent years.[5] Many patients with prostatism have serious arteriosclerotic heart disease and cannot tolerate rapid changes in vascular volume. The condition of these patients presents a major problem of management. The question arose as to how much irrigating fluid is absorbed into the vascular system during a carefully performed transurethral resection, with use of a low hydrostatic fluid pressure and dissection only to the superficial fibers of the surgical capsule. Previous studies with use of radioisotopes indicated that as much as 3.5 to 4 liters of irrigating fluid may be absorbed in some cases.[6] The absorption of a volume of fluid of this magnitude would appear to be hazardous in many cases.

Radioisotopes afford a means of labeling both irrigating fluid and red blood cells for determination of fluid absorption and hemolysis respectively. Griffin,[6a] using radioisotopes as a labeling agent in the irrigating fluid, reported as much as 4 liters of absorption. Taylor [6b] and associates, using a variation of this method, estimated that as much as 3,400 ml. of fluid may be absorbed into the vascular system during resection. One of their patients died from pulmonary edema after absorption of 2,900 ml.

Thus, while quantitative determination of hemoglobinemia has previously been made during transurethral resections with use of sterile water as the irrigant,[7] hemolysis has not been measured before by means of radioisotopes. One of us (L. O. G.) has now devised a technique of measuring hemolysis quantitatively with use of radioisotopes.

Purpose of Study

The purpose of this investigation was to measure fluid absorption, hemolysis, and blood loss in the ordinary transurethral prostatectomy in which a low irrigating pressure is used and the dissection is limited to the superficial fibers of the surgical capsule. In most cases the larger venous sinuses are not encountered, as they lie deeper, near the true capsule. The primary object was to determine whether irrigating fluid would be absorbed in

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From the Santa Fe Hospital.

amounts sufficient to be expected to cause cardiac strain. Secondary objectives were to determine how much hemolysis occurs with the use of sterile distilled water as the irrigant, and to measure blood loss during the operation.

Subjects and Procedures

The subjects of our study were patients with prostatism selected as candidates for transurethral prostatectomy at the Santa Fe Hospital, Topeka, Kan. Fluid absorption was measured in 11 patients, hemolysis determined in 9 patients, and loss of blood measured in 6 patients.

The operating procedure was identical in all cases. General anesthesia was used, consisting primarily of thiopental (Pentothal) sodium and succinylcholine chloride. The irrigating fluid was measured into an 8,000-ml. percolator. The hydrostatic pressure ranged from 40 to 75 cm. above the pubis. The bladder was emptied frequently to avoid overdistention. The number of liters of water used ranged from 7.5 to 18 liters, with an average of approximately 11 liters. In the 11 cases in which fluid absorption was measured, a solution of a concentrated, nonhemolytic urologic irrigating fluid, Cytal solution, was added to create a nonhemolyzing solution. (Each 100 cc. of Cytal, when diluted with 9 parts distilled water, contains sorbitol, 2.70 Gm.; mannitol, 0.54 Gm.; methyl parahydroxybenzoate, 0.5 mg.; propyl parahydroxybenzoate, 0.1 mg.; and butyl parahydroxybenzoate, 0.1 mg.) Sterile distilled water was used when hemolysis was measured, with the exception of one test case in which a nonhemolyzing solution was used as the irrigant.

Fulguration was employed minimally. The dissection of the adenoma was stopped at the fibers of the surgical capsule. The venous sinuses lying deeper in the capsule were rarely encountered. Operating time measured generally 60 minutes or less, with few exceptions. A 24 French Foley-Alcock catheter was used for continuous postoperative drainage. The bladder was not irrigated postoperatively. No complications developed in this series of patients.

Materials and Methods

The materials used in this study were radio-iodinated (I^{131}) serum albumin (human) (Risa) and sodium radio-chromate (Cr^{51}) (Rachromate). Absorption of irrigation fluid was determined by mixing the radioactive material with the irrigant and comparing the total radioactivity in the circulating blood at the end of the operation with the radioactivity in a given volume of the irrigant. Radio-iodinated (I^{131}) serum albumin (human) was used in 6, and sodium radio-chromate (Cr^{51}) in 5 of the 11 cases.

Hemolysis was measured by tagging the red blood cells with sodium radio-chromate (Cr^{51}) and comparing the total gain in radioactivity in the circulating plasma during the operation with the radioactivity in a given volume of packed red blood cells. The blood volume and hematocrit of each patient was measured.

Method for Determination of Fluid Absorption.—From 25 to 40 μc of radio-iodinated human serum albumin was added to about 16 liters of Cytal solution. The activity in the irrigant was determined by counting 4-ml. specimens in duplicate. Some difficulty was encountered because the pH of the distilled water used approached the isoelectric point of serum albumin, resulting in an uneven distribution of the radio-iodinated serum albumin in the irrigant. At about 20-minute intervals during the operation, 4-ml. blood specimens were drawn and the radioactivity determined. The blood volume was measured after surgery, also with use of radio-iodinated serum albumin. The volume of irrigation solution absorbed, in milliliters, was computed by dividing the total radioactivity absorbed in the blood by radioactivity per milliliter of irrigant.

Method for Determination of Hemolysis.—Approximately 40 ml. of blood was withdrawn from the patient and injected into a sterile, silicone-treated bottle containing 10 ml. of special formula A. C. D. solution. From 50 to 200 μc of sodium radio-chromate (Cr^{51}) was added. Ascorbic acid, 50 to 100 mg. was added to stop the tagging of the red blood cells and to tag the plasma for blood volume determination. In order to obtain reasonable tagging of the plasma, it was necessary to add the vitamin in less than one minute. All but 12 to 15 ml. was withdrawn into a sterile syringe, weighed, and injected into an antecubital vein. The remaining blood was used to determine the hematocrit of the injected blood and to prepare a whole blood and a plasma standard. The red blood cell volume and plasma volume were calculated from the hematocrit and from the radioactivities in 15-minute specimens of whole blood and plasma and in the standards.

The operation was performed six or seven days later, when plasma activity was nearly negligible. Pure distilled water was used as the irrigant. Blood specimens were taken at about 20-minute intervals during the operation and immediately thereafter.

Measurement of hemolysis requires that the activity per unit volume of packed red blood cells be determined. This activity compared with the total increase in activity in the plasma gives a measurement of cells hemolyzed.

Determination of the radioactivity per unit volume of packed red blood cells cannot be done directly, because the volume of red blood cells counted cannot be accurately measured. Red blood cells cannot be entirely freed from plasma and they stick to the surface of volumetric glassware.

With Kaplan's indirect method[8] the activity per unit volume of packed red blood cells can be simply and accurately determined by use of the microhematocrit of the whole blood specimen, 4 ml. of hemolyzed whole blood, and 4 ml. of clear plasma. The whole blood is thoroughly mixed, and 4 ml. is measured into a plastic counting test tube with a volumetric pipet and hemolyzed by setting the test tube in water at about 70 C for two or three minutes. Thorough mixing of the whole blood is essential for accurate measurement of the microhematocrit. Two capillary tubes are used and the results averaged. After centrifuging the remaining blood, a 4-ml. aliquot of clear plasma is measured with a volumetric pipet, as before.

That part of the net counts per minute in the whole blood due to plasma in the specimen is equal to the net counts per minute in the 4-ml. specimen of clear plasma times the difference between one and the microhematocrit, called the plasmacrit. The volume of red blood cells in the 4-ml. specimen of whole blood is equal to the microhematocrit times 4 ml. The net counts per minute in this volume of red blood cells are equal to the net counts per minute of the whole blood specimen, less the net counts per minute due to the plasma in the specimen. Dividing by the volume of red blood cells gives the activity per milliliter of packed red blood cells. The equation for the above is as follows:

$$R_c = \frac{R_w - R_p(1 - H_c)}{4 \times H_c}$$

where R_c = net counting rate per milliliter of packed red blood cells
R_w = net counting rate of a 4-ml. sample of whole blood
R_p = net counting rate of a 4-ml. sample of clear plasma
H_c = microhematocrit

The determination of total hemolysis caused by sterile distilled water during the operation depends on the determination of plasma volume and the tagging of red blood cells with a radioisotope. Sodium radio-chromate (Cr^{51}) was used to simultaneously tag the red blood cells and measure the plasma volume, either directly by tagging the plasma or indirectly by using the venous hematocrit, with either the whole blood volume or the red blood cell volume. Tagging the plasma yields accurate results, but several days must elapse between the plasma volume determination and the operation, in order that the plasma activity may be eliminated. Thus, change in plasma volume may occur before the time of surgery.

Determination of Blood Loss.—A logical method for simultaneous determination of absorption and blood loss was tried. The irrigant is either absorbed or excreted. The total fluid excreted is composed of blood lost, a very small amount of urine, and the excreted irrigant. The ratio of the radioactivity per unit volume of the fluid excreted to that of the irrigant, times the total volume excreted, gives the volume of irrigant in the excreted fluid. Subtraction of this volume from the volume of irrigant gives the absorption, and from the total fluid excreted gives the volume of blood and urine excreted.

Collection of all of the excreted fluid was a problem. A rubber sheet was used to funnel the fluid into the collecting tray, from which the fluid flowed into a carboy. Estimates of loss of this fluid, such as on the surgeon's gown, ranged from 30 to 200 ml. The average blood loss by six patients (table 2) was less than 280 ml. as determined by a direct isotopic dilution technique. Because the error in determining the excreted volume was approximately of the same order as the blood loss and irrigant absorption, the simultaneous volume technique was abandoned.

Blood loss during the operation was determined in six out of nine cases by collecting the excreted fluid of patients whose red blood cells had been tagged with sodium radio-chromate (Cr^{51}) several days before the operation, determining the total radioactivity of the fluid, dividing by the activity per milliliter of red blood cells, and dividing the result by the hematocrit of the patient during the operation (table 2). In this method, errors in measuring the volume of the excreted fluid are relatively unimportant. They are proportional to the ratio of the volume error to the total volume of fluid excreted.

Of considerable importance is the error in the hematocrit. Venous hematocrits were determined. Whole body hematocrits are known to average about 91 or 92% of the venous hematocrit[9] and may range from about 80 to 100%. It seems probable, therefore, that the blood losses reported in table 2 are at least 10% too low. However, the volume of packed red blood cells lost can be quite accurately determined.

A possible source of error is the comparatively rapid elimination of sodium radio-chromate (Cr^{51}) from the plasma. This may be important in two ways. First, we did not take multiple blood specimens and extrapolate back to determine the plasma activity at zero time, as recommended by Kaplan.[8] This would tend to make our plasma volume determinations too high. Second, a significant part of the activity released into the plasma by hemolysis may have been removed from the circulation by the liver and kidneys before the operation was completed. This would tend to make our plasma activity measurement too low. Fortunately, these effects tend to balance each other in the hemolysis determination.

Radio-iodinated serum albumin appears to be removed from the circulating plasma, but at a lower rate. In a supplementary investigation, three patients in whom a loss of about 10% of the circulating radio-iodinated serum albumin occurred were observed for two hours. This would tend to make our absorption measurements too low.

Data

Fluid Absorption.—In 7 of the 11 cases investigated, intravascular fluid absorption measured less than 110 ml. (table 1). Significant fluid absorption occurred in one case. In case 5, in which the operating time was extended to 90 minutes, 1,780 ml. was absorbed. In this case, venous sinuses were opened. Discounting this case, the over-all average absorption per case measured 237 ml.

Hemolysis.—Pure distilled water was used as the irrigation solution in eight cases (table 2). In the ninth case a Cytal solution was used. Hemolysis was measured as milliliters of packed red blood cells hemolyzed. This was also expressed as the percentage of the total red blood cell volume hemolyzed. The average volume of packed red blood cells hemolyzed measured 11 ml., with a range from 0 to 44 ml. Hemolysis did not occur in one case in which sterile water was used as the irrigating solution. This was a 7-Gm. resection for carcinoma. In the test case (case 20) in which a nonhemolyzing irrigating solution was used, hemolysis could not be detected, although 40 Gm. of tissue had been resected and the operation required 70 minutes.

TABLE 1.—*Radioisotopic Determination of Irrigating Fluid Absorption in Transurethral Prostatectomy**

Case No.	Weight of Tissue Resected, Gm.	Time of Resection, Min.	Blood Volume, Ml.	Radioactivity of Irrigant, Counts/Min./Ml.	Radioactivity of Whole Blood, Postoperative, Counts/Min./Ml.	Volume of Irrigant Absorbed, Ml.
1............	33	45	5,050	1,319	19.0	84
2............	22	60	4,050	2,732	239	353
3............	11	50	5,120	2,722	64.8	103
4............	11	40	5,500	1,777	34.5	100
5............	32	90	5,360	791	263	1,780
6............	41	70	5,380	706	30.3†	299
7............	9	30	6,810	465	2.75	40
8............	21	45	5,690	584	0	0
9............	15	45	5,610	592	132	1,230
10............	23	45	5,960	681	5.5	48
11............	30	45	5,080	603	12.3	103

* In cases 1 through 6 the irrigant was labeled with radio-iodinated (I^{131}) serum albumin (human) 40μc, and in cases 7 through 11 with sodium radio-chromate (Cr^{51}). In all cases the pathological condition was benign prostatic hypertrophy.

† Maximum activity occurred before end of surgery.

TABLE 2.—*Radioisotopic Determination of Hemolysis and Blood Loss During Transurethral Prostatectomy*

Case No.	Pathology	Cr^{51} to Tag Cells, μc	Weight of Tissue Resected, Gm.	Time of Resection, Min.	RBC Volume, Ml.	Plasma Volume, Ml.	Gain in Plasma Radioactivity, Counts/Min./Ml.	Av. RBC Radioactivity, Counts/Min./Ml.	Packed RBC's Hemolyzed, Ml.	Total RBC Volume, Hemolyzed, %	Blood Loss, Ml.
12	Benign prostatic hypertrophy ..	200	33	45	1,950	2,690	29.0	7,238	10.8	0.55	345
13	Cancer	100	15	45	1,560	2,110	7.75	4,802	3.4	0.22	262
14	Benign prostatic hypertrophy ..	200	9	55	1,765*	2,015*	3.83	7,902	0.98*	0.055*	86
15	Benign prostatic hypertrophy ..	100	29	60	2,195	2,855	4.25	3,797	3.2	0.15	396
16	Benign prostatic hypertrophy ..	100	25	50	2,290†	2,910†	13.0	3,840†	9.9†	0.43†	521
17	Cancer	100	7	60	2,160	2,570	0.0	1,787	0.0	0.0	55
18	Benign prostatic hypertrophy ..	50	9	25	2,415	2,880	3.4	629	15.6	0.65	...§
19	Benign prostatic hypertrophy ..	50	29	55	2,255‡	2,875‡	5.2	339‡	44‡	1.95‡	...§
20‖	Benign prostatic hypertrophy ..	50	40	70	...§	...§	0.0	919	0.0	0.0	...§

* Blood volume 3,780 ml. Hematocrit in question.

† Hematocrit 44.0%. Blood volume determination inaccurate. Theoretical blood volume used.

‡ Hematocrit 44.0%. Doubtful that all of tagged cells were reinjected into lumen of antecubital vein. Theoretical blood volume used.

§ Not determined.

‖ Cytal, nonhemolytic irrigant. Pure distilled water used for other cases.

Comment

Radioisotopes were used as a labeling agent in 11 cases to measure fluid absorption, in 9 cases to measure hemolysis, and in 6 cases to measure bleeding during transurethral resection of the prostate. The standard recommended operative technique for transurethral prostatectomy was followed. The measures employed in this procedure to limit fluid absorption include the use of a low hydrostatic fluid pressure, frequent emptying of the bladder, restriction of operating time to approximately 60 minutes, and limiting dissection to the superficial fibers of the surgical capsule of the prostate.

The primary objective of the study was to determine whether sufficient fluid is absorbed under these conditions to strain a weakened myocardium. Secondary objectives of this investigation were the quantitative determination of hemolysis resulting from the use of sterile distilled water as the irrigant, and measurement of blood loss.

Only one patient showed what would appear to be excessive absorption. In this case, 1,780 ml. of fluid was absorbed. It should be noted that in this case the operating time was prolonged to 90 minutes, and the operator felt that venous sinuses had been opened. The patient exhibited no untoward reaction, such as elevated blood pressure, or other effect. In general, fluid absorption was considerably less than one liter, an amount which would appear to be without clinical significance.

Hemolysis was measured by tagging red blood cells with sodium radio-chromate (Cr^{51}) and measuring the total increase in radioactivity of the plasma during surgery. Hemolysis was measured as milliliters of packed red blood cells hemolyzed, and expressed as the percentage of the total red blood cell volume hemolyzed. The largest volume of red blood cells hemolyzed measured 44 ml., in a patient who exhibited no ill-effects. In the other cases the volume of redblood cells hemolyzed measured less than 16 ml. Hemoglobinemia secondary to the hemolysis of this small volume of red blood cells would appear to be of no clinical significance.

Bleeding was measured in six cases by determining the total radioactivity in the excreted fluid of patients whose red blood cells had been tagged with sodium radio-chromate (Cr^{51}), and dividing by the product of the hematocrit and the activity per milliliter of red blood cells. Blood losses ranged from 55 to 521 ml. and averaged less tha

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15	Benign prostatic hypertrophy ..	100	29	60	2,195	2,855	4.25	3,797	3.2	0.15	396
16	Benign prostatic hypertrophy ..	100	25	50	2,290†	2,910†	13.0	3,840†	9.9†	0.43†	521
17	Cancer	100	7	60	2,160	2,670	0.0	1,787	0.0	0.0	55
18	Benign prostatic hypertrophy ..	50	9	25	2,415	2,880	3.4	629	15.6	0.65	...§
19	Benign prostatic hypertrophy ..	50	29	55	2,255‡	2,875‡	5.2	339‡	44‡	1.95‡	...§
20‖	Benign prostatic hypertrophy ..	50	40	70	...§	...§	0.0	919	0.0	0.0	...§

* Blood volume 3,780 ml. Hematocrit in question.

† Hematocrit 44.0%. Blood volume determination inaccurate. Theoretical blood volume used.

‡ Hematocrit 44.0%. Doubtful that all of tagged cells were reinjected into lumen of antecubital vein. Theoretical blood volume used.

§ Not determined.

‖ Cytal, nonhemolytic irrigant. Pure distilled water used for other cases.

Comment

Radioisotopes were used as a labeling agent in 11 cases to measure fluid absorption, in 9 cases to measure hemolysis, and in 6 cases to measure bleeding during transurethral resection of the prostate. The standard recommended operative technique for transurethral prostatectomy was followed. The measures employed in this procedure to limit fluid absorption include the use of a low hydrostatic fluid pressure, frequent emptying of the bladder, restriction of operating time to approximately 60 minutes, and limiting dissection to the superficial fibers of the surgical capsule of the prostate.

The primary objective of the study was to determine whether sufficient fluid is absorbed under these conditions to strain a weakened myocardium. Secondary objectives of this investigation were the quantitative determination of hemolysis resulting from the use of sterile distilled water as the irrigant, and measurement of blood loss.

Only one patient showed what would appear to be excessive absorption. In this case, 1,780 ml. of fluid was absorbed. It should be noted that in this case the operating time was prolonged to 90 minutes, and the operator felt that venous sinuses had been opened. The patient exhibited no untoward reaction, such as elevated blood pressure, or other effect. In general, fluid absorption was considerably less than one liter, an amount which would appear to be without clinical significance.

Hemolysis was measured by tagging red blood cells with sodium radio-chromate (Cr^{51}) and measuring the total increase in radioactivity of the plasma during surgery. Hemolysis was measured as milliliters of packed red blood cells hemolyzed, and expressed as the percentage of the total red blood cell volume hemolyzed. The largest volume of red blood cells hemolyzed measured 44 ml., in a patient who exhibited no ill-effects. In the other cases the volume of redblood cells hemolyzed measured less than 16 ml. Hemoglobinemia secondary to the hemolysis of this small volume of red blood cells would appear to be of no clinical significance.

Bleeding was measured in six cases by determining the total radioactivity in the excreted fluid of patients whose red blood cells had been tagged with sodium radio-chromate (Cr^{51}), and dividing by the product of the hematocrit and the activity per milliliter of red blood cells. Blood losses ranged from 55 to 521 ml. and averaged less than 280 ml.

This study suggests that fluid absorption is n excessive during transurethral resection of the tate if a low hydrostatic fluid pressure is throughout and the dissection is not carried into the venous sinuses lying deep in the surgical capsule.

The study of hemolysis would indicate that sterile distilled water is a safe irrigating medium if used properly. One of us (E. M. F.) does not feel that an iso-osmotic solution adds to the difficulty of resection. It has a great added advantage in reducing toxicity in the event of perforation of the surgical capsule.

109 W. Ninth St. (Dr. Fillman).

The A. C. D. solution used in this study was a special formula supplied by Abbott Laboratories, North Chicago, Ill. The radio-iodinated (I^{131}) serum albumin (human) and the sodium radio-chromate (Cr^{51}) were supplied as Risa and Rachromate, respectively, by Abbott Laboratories.

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TREATMENT OF CHRONIC ALCOHOLISM BY HYPNOTIC AVERSION

Michael M. Miller, M.D., Washington, D. C.

Hypnosis has been used in 24 patients with chronic alcoholism to create an aversion to alcoholic drinks. The duration of the alcoholism ranged from 3 to 34 years, and the patients were made to relive the unpleasant hang-over effects of alcohol in the hypnotic trance. During the follow-up period, which averaged nine months, four patients relapsed, one of whom has so far responded well to additional treatment. Three case histories illustrate the favorable results obtained in two men aged 45 and 53 and a woman aged 56.

For some time I have been experimenting with various methods in an attempt to create a lasting aversion to alcoholic spirits by means of hypnosis. Since the smell and taste of whiskey, beer, and wine are generally pleasurable to the alcoholic, I felt that it was necessary to attempt to create an aversion to the taste, smell, and thought of alcoholic beverages and, furthermore, that if the generally pleasant anticipatory reaction of the alcoholic to alcoholic beverages could be altered to one of disgust and displeasure, it would discourage any primary desire for drink. In my initial attempts, I found that the aversion reactions could be intensified by having patients relive the unpleasant "hang-over" effects of alcohol in the hypnotic trance.

The basic rationale was that of Freud's pleasure principle and the efforts of the unconscious mind to evade or avoid reliving a painful, disgusting, or disagreeable experience. Pavlov[1] had demonstrated how conditioned reflexes could be established and how reactivity could be so intensified that a light stimulus would produce a marked response. It was known that the phenomenon of hypnosis resembles a conditioned response in that the subject becomes increasingly susceptible to hypnotic induction (phenomenon of "dressage"). Thus, it appeared similarly possible to "sensitize" and accelerate reflex response by means of hypnosis.

From Howard University Medical School.

Even a slight whiff or taste of alcoholic beverages might be sufficient to evoke a conditioned aversion reaction.

Attempts along this line on the conscious level have been made by other investigators in the so-called conditioned reflex aversion treatment of alcoholics, by Voegtlin[2] and LeMere and co-workers.[3] In these instances the subjects were given alcoholic spirits after a nauseant and an emetic drug, generally emetine hydrochloride, had been administered. The result was that the patient would become nauseated and vomit the ingested alcohol. The purpose was to create an aversion, based on taste and smell, to alcoholic beverages. This was repeated for a number of treatments until the therapist was satisfied that the patient had an aversion to alcohol. I should like to comment briefly on this mode of treatment. Dercum[4] deprecated the use of such depressant and nauseant drugs as emetine and apomorphine in the treatment of alcoholism, considering the treatment as possibly harmful and of little lasting benefit. Certainly the treatment is not without its dangers and is, because of its duration, a painful experience for the patient. No doubt there has been some success with this method, although longer follow-up data on results obtained have been difficult to secure. The one important drawback in the treatment is that the patient is usually aware that he is being given an injection of a nauseant drug when the spirits are administered. If we are to assume that the patient associates the vomiting with taking the whiskey, why could it not just as readily be assumed that he is as likely, if not more likely, to associate the vomiting with the injection? Illustrative of this type of reaction was a 32-year-old alcoholic woman whom I encountered some years ago at the Cleveland House of Correction. She had just completed a "wonder cure" at the Greenhill Institute there. It appeared that her husband had mortgaged the family car so that she could have the treatment. When I asked her why she had begun to drink again, after her husband had made such a sacrifice to have her treated, she remarked, "But, doctor, after they made me puke for three days and three nights, I just had to have some whiskey to settle my stomach."

With reference to the use of disulfiram (Antabuse)[5] one must also be aware of certain problems. There are persons who may present a toxic sensitivity to the drug. Undesirable side-effects such as drowsiness, mild grand mal convulsions, gastrointestinal complaints, fatigue, headache, dizziness, and diminished sexual potency have been reported.[6] The treatment is generally contraindicated in the presence of diabetes, renal disorders, liver diseases, and epilepsy. It is particularly hazardous to cardiac and hypotensive patients who drink while taking disulfiram. There have been instances when compulsive, self-destructive, suicidal drinkers have consumed alcoholic spirits while under the influence of disulfiram and suffered severe reactions, as would be anticipated. In some instances such reactions could be fatal.

Many alcoholics will take disulfiram for a brief period and discontinue its use whenever they feel a desire to go on another drinking spree. The principal deterrent to the use of disulfiram is the fear that it engenders in the patient. Frequently, patients taking disulfiram may demonstrate a prevailing tension or manifest anxiety concerning the possible consequences, should they yield to the desire to drink.

My decision to experiment with hypnosis in attempting to create an aversion was based on a number of considerations. First and foremost, I felt that one of the greatest weaknesses of the aforementioned treatment was that it was on a conscious level. It appeared likely that the aversion and disgust reaction could be prolonged and intensified if a conditioned-reflex reaction could be established in the unconscious mind of the patient and, furthermore, that in order for this aversion to persist it had to be established beyond the reach of conscious resistances and ego defenses. In addition, it was desirable to avoid the use of possibly dangerous nauseant and depressant drugs. The advisability of submitting patients who are often seriously nutritionally depleted to daily emesis for 7 to 10 days can frankly be questioned. It was also apparent that, if successful, the hypnotically induced reflex aversion could be established much more rapidly and effectively, without causing the patient as much discomfort and dread of the treatment.

It was felt that the aversion reaction could be made more intense and lasting to the patient because of the greatly increased state of affectivity under hypnosis. It appears preferable for all concerned to be able to create a disgust aversion reflex reaction in a painless manner, so that the patient experiences a lack of appetite and desire for alcoholic beverages. Obviously, such a patient will not consume alcoholic beverages if he derives no pleasure from them and actually finds that the smell, taste, and sight of alcohol upset him physically and emotionally. Finally, such a treatment could be easily given on an outpatient basis and would not require the hospitalization of the person and the loss of time and expense involved.

Evaluation of Results

This is merely a preliminary report and covers a relatively small group of patients. Most of these patients were seen at the Howard University neuropsychiatric clinic, the remainder at my office. Of the 24 patients treated thus far, 5 were women. The duration of their alcoholism ranged from 3 to 34 years. The average time of follow-up has been nine months. Eighteen of these patients are continuing psychotherapy. The average number of treatments received was two, but in some instances a third or fourth treatment was given if indicated. Eight attend Alcoholics Anonymous meetings. Of the total, three patients have relapsed thus far. The criterion employed was that of continued abstinence from alcoholic beverages. About half of the patients made attempts to test themselves with alcohol, and all of these developed prompt aversion reactions and discontinued further such attempts. One of the patients attempted to drink beer after an aversion to whiskey only had been initiated. One first switched to barbiturates and then became intoxicated after the ingestion of larger doses of barbiturates. The third patient was disturbed, with a marked tendency toward depression.

No claims are being made for this treatment as a cure-all for alcoholism. It represents only a procedure for attempting to control drinking so that constructive psychotherapeutic, social, and economic rehabilitative steps can be taken. Alcoholism is symptomatic of deeper underlying disturbances of the personality, and there are probably as many diverse causes for alcoholism as exist for human unhappiness.

Procedure

In most instances I have found it sufficient to follow the initial treatment with a second aversion treatment a week later. Further treatment is usually unnecessary unless indicated by a tendency on the part of the patient to relapse. After the initial treatment patients may often test themselves with alcoholic beverages. If properly conditioned under hypnosis, they will promptly become nauseated and frequently vomit any ingested spirits. If the patient is in a poor nutritional state or in need of medical care or hospitalization, posthypnotic suggestion can be used to advantage to facilitate his cooperation in remedial measures. It is advisable to use posthypnotic suggestion further and influence the patient against the use of sedative drugs and tranquilizers as a substitute for the alcohol. The dangers of this practice should be strongly stressed. Alcoholics are particularly apt to develop dependency on habit-forming sedative drugs, since they are generally suffering from marked inner anxieties and guilt. As aforementioned, psychotherapeutic measures should be strongly encouraged at this point and posthypnotic suggestion utilized toward attaining this goal, since the underlying personality and character problems have not been resolved.

The hypnoreflex aversion treatment presents certain other advantages. It is completely harmless in the hands of a properly trained psychotherapist. Furthermore, since it is administered under hypnosis, it is possible to keep the patient consciously relatively unaware of any painful or disagreeable nauseating or vomiting experiences. This treatment can easily be administered to ambulant patients and does not require hospitalization. Since the aversion is created at an unconscious level, it is more intense and lasting. In addition, it provides the opportunity, while the patient is in the hypnotic trance, to explore some of the principal problems and conflicts which may underly his alcoholism and to permit him to abreact his emotional tensions. It also affords the opportunity to influence the patient to pursue a constructive medical, social, and psychotherapeutic regimen[7] by the skillful employment of posthypnotic suggestion. It is often possible to better evaluate the patient's problems with regard to whether he should undergo individual or group psychotherapy. Also, under hypnosis, the patient can relive his most disagreeable "hang-over" experiences intrapsychically, without having to ingest alcohol or nauseant drugs.

As aforementioned, the hypnotic reflex aversion treatment is far more effective because the aversion is created while the subject is unconscious and cannot employ his ego defenses or resistances. There is a stronger affective component in the latter instance, because affectivity is markedly increased while intellectualization is markedly diminished under hypnosis. The discussed aversion reaction is therefore felt by the patient with greater intensity. Furthermore, because of hypnotic amnesia, he is unable to link or correlate the aversion reaction with any administration of a medicament to induce it. In most instances, I simply intensify the disgust, aversion, and displeasure of the hang-over state by having the subject actually relive one of his worst hang-overs.

It is important, as indicated earlier, to create, if possible, an aversion reaction to all types of spirits, including beer and wine, since I have seen instances in which a patient was given an aversion treatment to whiskey only and then attempted to switch to beer or wine in order to satisfy his craving. During the trance, it is also advisable to stress the dangers of switching the dependency to sedative drugs, such as barb[illegible]ates and tranquilizers, while on the other har[illegible]ng constructive measures.

It i[illegible]ent that this treatment should be [illegible]y a psychotherapist who is well [illegible]hypnosis. Hypnotherapy is a method that [illegible]quires adequate comprehension of the dynamics of the unconscious mind. Much harm can be done by its misuse, and it must be used only with specific medical indication, never indiscriminately.

Treatment is first explained to the patient as harmless, and no attempt is made to force the patient to undergo it. Cooperation should be on a completely voluntary basis.

I have found that aversion reactions by means of hypnosis can be successfully induced in the treatment of such conditions as obesity (aversion to specific foods), compulsive cigarette smoking, and certain instances of drug addiction. This technique has been effective in treating obesity in diabetic patients.

Summary of Cases

Case 1.—A 45-year-old man became an alcoholic at about 20 years of age. He began drinking at the age of 16 years. His drinking followed a compulsive pattern, and after severe bouts he would become depressed. During such postalcoholic depression states he twice attempted suicide, once by hanging himself with a belt. The patient gave a typical picture of latent repressed homosexuality; homosexual men particularly tended to disturb him greatly. He suffered from partial impotence and had strong feelings of inferiority, guilt, and self-condemnation, particularly manifest during his hang-overs and brief intervals of abstinence.

He felt that alcohol relieved his tension and made him feel more masculine and less aware of the effeminate component in himself. When drinking, he would release his pent-up self-hate on others, acting hostile, becoming enraged at the slightest provocation, and being disagreeable and negativistic. He described his alcoholism as a "crutch" on which he could always lean when he felt bad: "I would just wipe out reality for about two weeks."

My endogenic method of hypnotic relaxation[8] was employed, and the patient was in a deep trance within three minutes. He was then made to relive his worst hang-over, including the malaise, headache, nausea, and vomiting. He began emesis in four minutes after strong suggestions were given, while at the same time he was permitted to smell and taste whiskey, wine, and beer.

He was given specific suggestion that, whenever he tasted, smelled, or even looked at alcoholic beverages, he would begin to recall these horrible hang-over symptoms. This patient has been abstinent for 12 months at the time of writing. He states that he cannot anticipate any pleasure at the taste, smell, sight, or even thought of alcoholic beverages. During this period he has been treated by group psychotherapy twice weekly, and he is making excellent progress in resolving his basic difficulties.

Case 2.—A 56-year-old woman had been a chronic alcoholic since her husband's death eight years earlier. Prior to that, she stated, she had drunk only socially and had never experienced alcoholic intoxication.

The patient stated that she felt a compulsion to drink, even though at times she had desired to abstain but was unable to do so. She was relaxed by the endogenic method within four minutes and then given aversion conditioning treatments similar to those given in the previous case. This patient did not have an emesis but felt very nauseated.

She has been completely abstinent for 11 months at the time of writing. She has complete aversion to the taste and smell of alcoholic beverages. These not only evoke a disagreeable nauseous feeling rapidly but also are promptly associated by the patient with disagreeable "hang-over" feelings.

Case 3.—A 53-year-old man had been affiliated with Alcoholics Anonymous for eight years but was unable to curb his drinking. He had been drinking excessively for approximately 30 years. Under hypnosis he revealed that he had suffered from severe feelings of inadequacy as a man and that alcohol made him feel more "manly." The patient revealed further that he was a minister's son and had been reared very rigidly. Sexual matters were never discussed at home and the patient had always been held up as a model boy for the congregation. He was constantly plagued by shame and guilt feelings. After puberty he became preoccupied with perverse and infantile sexual impulses and fantasies. He always felt guilty about these, and later in life he discovered that he could derive considerable relief for his guilt through drinking. His drinking bouts were followed by strong secondary guilt feelings, depression, and physical illness. This patient was given an aversion treatment under hypnosis. Two days after this, while under considerable mental tension, he went into a bar and ordered 2 oz. of vodka with orange juice. After ingesting this drink he became nauseated and had an emesis. He was given a second aversion treatment on the next day, and he has remained completely abstinent for nine months at the time of writing. Intensive psychotherapy was instituted in order to deal with his deep-seated neurotic problems. His guilt and anxiety feelings have greatly diminished, while his insight into his problems is greatly improved. He has been able to remain in his job, which is a position of responsibility. He also reports that his marital life generally has improved.

2025 Eye St., N. W. (6).

Addendum

Since this paper was submitted one additional alcoholic patient who received aversion treatment by hypnosis has relapsed. This patient received another aversion treatment after the relapse and has been abstinent for one month.

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EFFECTS OF CHLORPROMAZINE AND ALCOHOL ON COORDINATION AND JUDGMENT

George A. Zirkle, Ph.D., Peter D. King, M.D., Ott B. McAtee, M.D.
and
Robert Van Dyke, North Madison, Ind.

This study was designed to test the belief that simultaneous use of tranquilizing drugs and alcoholic drinks has a particularly bad effect on neuromuscular coordination and interferes with safety in automobile driving. A battery of tests was applied to 24 volunteer subjects under four experimental conditions achieved with combinations of alcohol and chlorpromazine, alcohol and placebo tablet, placebo drink and chlorpromazine, and placebo drink and placebo tablet. The effect of alcohol and chlorpromazine taken together significantly impaired the performance of the subjects. The more complex tasks were most affected, and the subjects became aware of dulness, lethargy, and poor coordination. Chlorpromazine alone impaired performance, but the impairment caused by alcohol with chlorpromazine was significantly greater. Patients obliged to take chlorpromazine should be warned that the use of alcohol greatly increases the dangers of operating complex machinery, including automobiles.

This experimental study resulted from an observation on the part of certain police officers that a combination of tranquilizing drug and alcohol appeared to interfere with safe automobile driving more than did alcohol alone. Interrogation of an alcoholic disclosed the fact that he noticed a greatly increased effect from whiskey after having first taken meprobamate. However, Marquis and co-workers[1] found no potentiating effect of meprobamate on alcohol. Since less than 1 oz. of alcohol was used in their study, and no effort was made to adjust alcohol concentration to body weight, it is not surprising that little effect was noted. Moreover, the authors did not state whether the subjects took the alcohol on an empty or a full stomach. If the subjects had recently taken food, the rate of absorption of the alcohol would have been slowed down and the alcohol blood volume would have been quite low at the end of the 30-minute waiting period allowed before the start of testing.

Greenhouse and Pilot[2] reported that alcoholic subjects treated with reserpine who continued to drink stated they received a more powerful effect from the alcohol. On the basis of animal studies showing a potentiating effect of chlorpromazine (Thorazine) hydrochloride on alcohol, its makers warn physicians to take particular care in administering it to patients who may have a considerable amount of alcohol in their systems. Fazekas and co-workers[3] questioned that there is a synergistic action between chlorpromazine and alcohol. A letter from Fazekas indicated, however, that he suspects that there is a potentiating effect of chlorpromazine on alcohol.

Chlorpromazine is being taken by large numbers of discharged mental patients today. Many of these patients operate automobiles or other complex machinery, and they have access to alcoholic beverages. If there is a potentiating effect of chlorpromazine on alcohol, solid evidence for it should be discovered so that effective control measures may be instituted. At Madison State Hospital by far the most common drug being taken by outpatients is chlorpromazine. A study of dosages over a year's time showed the most common one for outpatients to be 200 mg. per day. It was therefore decided to use this drug for the present study in the dosage of 200 mg. per day.

Experimental Problem and Procedure

The experimental problem was defined in terms of the null hypothesis: There is no more effect on human coordination and judgment from a combined dosage of alcohol and chlorpromazine than from either of these drugs taken singly.

To answer this problem four experimental conditions were provided. These were (1) placebo condition ("chlorpromazine" placebo plus placebo drink), (2) chlorpromazine condition (chlorpromazine plus placebo drink), (3) alcohol condition ("chlorpromazine" placebo plus alcohol drink), and (4) chlorpromazine-alcohol condition (chlorpromazine plus alcohol drink). The four conditions were rotated in four different sequences. Subjects were divided into four subgroups of six, with each group being assigned a different sequence. Placebos, chlorpromazine, and alcohol were administered orally, a "blind" procedure being used.

Consulting Psychologist, Madison State Hospital, and Chairman of Department of Psychology, Hanover College (Dr. Zirkle); Clinical Director of Female Service and Director of Clinical Research (Dr. King); Superintendent and Chief Medical Director, Madison State Hospital (Dr. McAtee); and Sergeant and Director of Charlestown Post Laboratory, Indiana State Police (Sgt. Van Dyke).

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To approximate the therapeutic situation it was decided to administer chlorpromazine to subjects for a week before its effects were tested. Its presence was verified by a urine test.[4] When administration was stopped, a week was allowed for it to be dissipated from the system before testing was resumed. Subjects took tablets on arising and retiring for the entire experimental period.

Ninety-five per cent ethyl alcohol was given to subjects, on empty stomachs, in combination with lemon-lime–flavored carbonated water, sugar, mint leaves, and ice. A placebo drink of the same without the alcohol was given on two of the test days. Some subjects knew from its smell, taste, and effects when the alcohol was present. Amounts of alcohol given were adjusted to body weights in order to produce a blood level close to 0.05%. Theoretically, 30 cc. of ethyl alcohol per 150 lb. (68.2 kg.) of body weight will produce this level. Individual variables affect the physiological action so that the theoretical level can seldom be exactly achieved, however. An extra 10 cc. of alcohol per 68 kg. (150 lb.) was given to compensate for the amount consumed by the body during the 45 minutes to an hour which elapsed before testing.

The 0.05% blood alcohol level was chosen because statutes in many states hold that this concentration does not impair driving ability. If chlorpromazine increased the action of this amount of alcohol to the point where the drinker's coordination and judgment were definitely impaired, then the supplementing or potentiating effect would be clearly demonstrated.

Subjects were allowed 15 minutes in which to drink the test beverage, and 45 minutes more were allowed for the desired concentration of alcohol to build up. They were then tested for blood alcohol volume by means of a Breathalyzer. This instrument operates on the principle that at body temperature the ratio between breath alcohol and blood alcohol is 2,100 to 1. Breath tests were made regardless of whether the subject had taken a drink containing alcohol. They were also made at the conclusion of the testing period on subjects who had taken alcohol.

Subjects.—Twenty-four subjects were enlisted for the experiment. Eighteen were employees at the hospital and six were patients. There were 18 men and 6 women, with ages ranging from 20 to 71 years. Most were in their 20's or 30's. Weights ranged from 105 to 210 lb. (48 to 96 kg.). Employees were informed that the experiment would involve the taking of chlorpromazine and alcohol and that it might help in making our highways safer. Three employee subjects were later dropped from the study, however, because of illness or failure to take the drug.

Because of the pressure of time the six patient subjects were chosen primarily because they were already taking 200 mg. of chlorpromazine per day and because they were relatively cooperative. They were given the same information about the experiment as employee subjects, except that no mention was made of chlorpromazine. A rerun of the experiment would dictate a more careful choice of patient subjects, as the participation of all was interfered with to some extent by their psychoses.

Tests Employed.—Because other investigators have found that routine, habitual, and reflex actions are little affected by low concentrations of alcohol, it was determined that more sensitive tests would need to be employed, tests which would call for the use of higher intellectual processes of coordination and judgment. It was presumed that these higher level processes would be more sensitive to the depressing or confusing effects of small amounts of alcohol.

The test battery selected comprised the following tests: (1) a digit-alphabet test requiring that letters be written below numbers according to a jumbled key—time limit 1½ minutes; (2) a tweezer dexterity test requiring that tweezers be used by the nonpreferred hand to insert 16 steel pins in a square of holes—timed; (3) counting backward by 1 from 100 for 30 seconds; (4) braking reaction time, with judgment, on an American Automobile Association Reaction Timer—subjects braked when a red light flashed but not when a green light flashed; (5) crossing out of groups of four dots randomly printed in rows with dot groups of other denominations—time limit 2½ minutes; (6) mental addition of 37 to lists of two-place numbers—time limit 1½ minutes; (7) differential lever pressing–reaction time to visual flashing of odd-odd and even-even digit combinations—odd-even combinations were also flashed, with the instruction that nothing be done when they appeared; and (8) matching the lengths of two lines in Mueller-Lyer and in vertical-horizontal illusions.

Specific tests were assigned to the three experimenters, who continued to administer the same tests throughout the project. Subjects were not informed of their test scores, although most had a fairly good idea of their success on some. Total testing time for the battery was approximately 20 minutes.

Results

Urine tests were positive for chlorpromazine in the two conditions involving its use. In the alcohol condition blood alcohol levels taken just prior to testing averaged 0.048%, with a standard deviation of 0.015. After testing the average was 0.038%, with a standard deviation of 0.010. In the alcohol-chlorpromazine condition blood levels prior to testing averaged 0.042%, with a standard deviation of 0.013 and after testing, 0.035%, with a standard deviation of 0.011.

Table 1 shows results under the four experimental conditions. Since the concern was for comparative results, raw scores in each condition are not shown. Instead, scores made on a test in all four conditions were added together to make a total score. Percentages of this total score were then computed for each condition. These percentages are given in table 1. Score percentages in each of the four conditions were ranked from 1 for best to 4 for worst. This was done since higher scores are better in some tests but worse in others. The *t* test was applied to differences in raw scores between the placebo condition and the other three conditions. The *t* values are also shown in the table.

It will be noted that performance was best under the placebo condition, with the highest average rank on the eight tests (1.6). Rank performance was worst under the alcohol-chlorpromazine condition (3.5). Ranks on the other two conditions were nearly the same. The *t* test showed a significant difference between scores on the placebo and alcohol-chlorpromazine conditions in the case of three tests. On one other test, counting backward, the *t* value of 2.06 is just short of significance at the 0.05 level. In the alcohol condition scores on two tests were significantly lower than in the placebo condition. In the chlorpromazine condition scores were significantly below those in the placebo condition on one test. Scores on the illusions test were significantly lower in the alcohol-chlorpromazine condition than in the alcohol condition ($p<0.05$). Scores on the counting backward test were significantly poorer in the alcohol-chlorpromazine condition than in the chlorpromazine condition ($p<0.05$).

Table 1.—*Comparison of Test Results of Twenty-four Subjects Under Four Experimental Conditions*

	Condition										
	Placebo		Alcohol			Chlorpromazine			Alcohol-Chlorpromazine		
Test	%	Rank	%	Rank	*t*	%	Rank	*t*	%	Rank	*t*
Digit alphabet	26.2	1	24.4	3	2.61*	25.3	2	1.13	24.1	4	2.23*
Illusions	23.3	2	22.7	1	0.11	26.2	3	1.23	27.9	4	2.29*
Tweezer dexterity	25.0	2	24.2	1	0.61	25.1	3	1.58	25.7	4	0.52
Counting backward	24.5	2	25.3	3	1.24	23.8	1	0.25	26.4	4	2.06
Braking time	24.9	3	24.8	2	0.31	24.7	1	0.39	25.6	4	0.52
Mental addition	27.9	1	24.7	2	2.13*	24.3	3	2.61*	23.1	4	2.50*
Choice reaction	23.1	1	25.8	3	1.80	26.1	4	1.18	25.0	2	1.18
Dot checking	26.1	1	24.2	4	1.75	24.6	3	1.41	25.1	2	0.58
Average		1.6		2.4			2.5			3.5	

*$p<0.05$.

While test results were affected by all three drug conditions, the greatest impairment must be attributed to the combination of alcohol and chlorpromazine. This is demonstrated in table 2, in which score percentages on all eight tests in the placebo condition are compared with like percentages in the three drug conditions.

In order to determine the effects of the drugs on judgment and reasoning the eight tests were ranked by the experimenters on the basis of the degree to which their mastery required higher intellectual ability. The resultant rank order in terms of increasing ability required was as follows: tweezer dexterity, braking reaction with judgment, dot checking, choice reaction time, illusion line matching, counting backward from 100, mental addition of two-place numbers, and digit-alphabet matching. The rank order of *t* values for each drug condition shown in table 1 were determined. Ranks in each condition were then correlated with the degree of judgment rank as noted above, with results shown in table 2.

When alcohol and chlorpromazine were taken in combination, the correlation noted is just short of significance at the 0.01 level. This indicates that the confusing or inhibiting effects of the combination increased with increasing need on the tasks for higher intellectual ability and judgment. In the case of the alcohol condition the correlation is just short of significance at the 0.05 level.

Results confirm the earlier view which dictated planning for tests to be used in this study; namely, that tests requiring higher and more complex mental abilities should be used rather than tests of routine or reflex activities. Mental activities of a higher intellectual variety are more subject to the effects of alcohol.

Subjective Data.—At the conclusion of each test period subjects were asked to register the excellence of their over-all performance on a 10-point scale, with 10 representing the best performance they would be capable of. Patient subjects had great difficulty in doing this, so the results from the 15 normal subjects only will be presented. The average ratings under the different conditions are shown in table 2. The *t* test was applied to differences between ratings in the placebo and three drug conditions.

These self-ratings closely parallel actual test results, as shown in table 1, and indicate that subjects realized their performance under the alcohol-chlorpromazine condition was not up to that under the other conditions. The difference between ratings under the placebo and alcohol-chlorpromazine conditions is highly significant.

Immediately after each test period the 15 employee subjects were asked to describe how they felt. After the alcohol-chlorpromazine session over 50% reported they were sleepy, and 40% reported feeling intoxicated or "groggy." These figures are twice as large as similar figures for the other three conditions combined. Peculiar to the alcohol-chlorpromazine condition also were such descriptions as "wobbly," "dizzy," "dull mentally," and "poorly coordinated"; almost half reported a lethargy described by two subjects as "not giving a damn." Three subjects spontaneously reported they got more effect from the alcohol on the day when they also had chlorpromazine. At the conclusion of the last experimental session, employee subjects were asked the following question: "If you had been driving an automobile instead of taking tests on the four test days, would there have been any one day when you would have been most unsafe as a driver?" Eighty-seven per cent picked the day on which they had both alcohol and chlorpromazine. The remainder chose the day when they received alcohol only.

TABLE 2.—*Comparison, Correlation, and Patient Evaluation of Results of Eight Tests Under Drug Conditions Versus Placebo Conditions*

	Drug Conditions		
	Alcohol	Chlorpromazine	Alcohol Plus Chlorpromazine
Comparison of composite score from all eight test results under placebo condition with test results under given drug condition			
t*	2.08	2.60	3.92
p	<0.10	<0.05	<0.005
Correlation between values of t and estimated degree of judgment required			
rho	0.619	0.154	0.827
p	<0.10		<0.05
Average self-ratings			
Rating†	6.4	6.3	5.5
t*	1.09	1.5	3.7
p	0.5	0.5	<0.01

* The t test was applied in each case to the difference between performance under placebo conditions and the given drug conditions.

† Ratings were on an arbitrary 10-point scale, with 10 representing the best possible performance. The three figures 6.4, 6.3, and 5.5 are to be compared with the average self-rating of performance under placebo conditions, which was 6.9.

Comment

The test results enabled us to reject the null hypothesis. As compared with the placebo condition, there was a significantly greater effect on coordination and judgment from a combined dosage of alcohol and chlorpromazine than from either of these drugs taken singly. In all eight tests employed, scores were worse in the alcohol-chlorpromazine condition than in the placebo condition. In the case of three tests, and almost so in the case of one other, the difference was significant at the 0.05 level of probability. When performance on all eight tests is compared, the difference is highly significant ($p<0.005$). Although performance was impaired in the alcohol condition, the degree of impairment was not nearly so great. This was true despite the fact that the average blood alcohol level in the alcohol condition (0.048%) was slightly higher than in the alcohol-chlorpromazine condition (0.042%). Although performance on the eight tests was impaired in the chlorpromazine condition ($p<0.05$), this impairment was less significant than in the alcohol-chlorpromazine condition ($p<0.005$).

A second interesting finding was the differential effect of the drugs on tasks requiring varying amounts of judgment and ability. Performance on higher level tasks was reduced in significantly greater degree than performance on lower level ones.

Greater impairment from the combination of drugs than from either one taken singly was recognized by the normal subjects, as indicated by their subjective ratings. Descriptions of their feelings while in the three drug states also revealed the greatest interference from the combination dosage.

Conclusions

Objective test data from all subjects and subjective evaluations from the normal subjects agree in pointing to a supplementary and possibly potentiating effect of chlorpromazine on alcohol in this experiment. In combination with chlorpromazine small amounts of alcohol were shown to significantly impair coordination and judgment, such as are needed for safe operation of automobiles and other complex machinery. It is therefore recommended that physicians who prescribe chlorpromazine should warn their patients of the possible dangers of the use of alcohol.

The placebos used in this study were supplied by Smith Kline & French Laboratories, Philadelphia.

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CLINICAL NOTES

EFFECT OF CIGARETTE SMOKING ON SERUM CHOLESTEROL AND LIPOPROTEIN CONCENTRATIONS

Irvine H. Page, M.D., Lena A. Lewis, Ph.D.
and
Mohammed Moinuddin, Ph.D., Cleveland

It has been suggested that cigarette smoking is in some way causally related to myocardial infarction and to coronary atherosclerosis. This is difficult to prove. Many investigators believe that the evidence is good for the association of hypercholesteremia and accelerated atherogenesis. If it could be shown that cigarette smoking is followed by a rise in serum cholesterol level, this could be interpreted as evidence in favor of a relationship of smoking and atherogenesis.

Methods of Study

The subjects of the present study were laboratory personnel. Fifteen were regular smokers; five were nonsmokers. A low-fat breakfast was eaten at about 7 a.m. The subjects refrained from smoking or taking fluids after 9 a.m. At 11:30 a.m. a control blood sample was taken, after which the subject smoked two nonfilter-tip cigarettes within a 10-minute period, inhaling deeply. Immediately, 10 minutes, and 30 minutes after the smoking was finished blood was collected. To determine the reproducibility of the procedure, three subjects (2, 11, and 12) were used on two occasions.

Table 1.—*Serum Cholesterol Concentration Before and After Smoking*

Subject No.	Cholesterol Level, Mg./100 Ml.: Presmoke	End of Smoke	10 Min. After End of Smoke	30 Min. After End of Smoke	Age, Yr.	Sex	Smoking History
1	213	184	190	227	31	M	Normally smokes about 1 pack nonfilter-tip cigarettes per day
2A	*	172	169	181	43	M	Normally smokes about 1 pack filter-tip cigarettes per day
B	172	167	165	162			
3	287	295	280	280	51	F	Normally smokes about 10 to 15 cigarettes (nonfilter) per day
4	325	329	319	323	42	M	Normally smokes about 15 to 20 nonfilter-tip cigarettes per day
5	178	188	191	179	23	F	Normally smokes about 1 pack filter tip, mentholated cigarettes per day
6	175	165	163	165	20	M	Normally smokes about 1 pack filter-tip cigarettes per day
7	174	179	171	171	21	M	Normally smokes about 1 pack filter-tip cigarettes per day
8	254	254	251	264	48	M	Normally smokes about 1 pack filter-tip cigarettes per day
9	192	191	198	188	29	M	Normally smokes about 1 pack filter-tip cigarettes per day
10	153	166	163	164	28	M	Normally smokes about 1 pack filter-tip cigarettes per day
11A	248	...	237	248	45	M	Nonsmoke control; does not usually smoke
B†	256	258	258	261			
12A	292	...	288	270	48	F	Nonsmoke control; does not usually smoke
B†	286	292	292	285			
13	228	224	227	231	34	F	Does not usually smoke
14	227	224	218	218	27	M	May not smoke cigarettes regularly; shifts to pipe for weeks
15	251	251	241	248	25	M	Smokes about 1 pack filter-tip cigarettes per day
16	176	170	...	...	17	F	Smokes about 1 pack filter-tip cigarettes per day
17	204	189	190	181	22	F	Smokes between ½ and 1 pack filter-tip cigarettes per day
18	273	278	271	278	47	F	Does not usually smoke
19	210	207	198	211	28	M	Does not usually smoke
20	194	198	190	188	21	M	Smokes between 5 and 10 cigarettes per day

* Lost.
† Smoked.

Two nonsmokers had blood drawn at intervals similar to those of the smokers. They breathed more deeply than usual for 10 minutes. The procedure was repeated when they smoked two cigarettes.

The serum cholesterol level was determined by the method of Abell and associates.[1] Serum lipoprotein levels were estimated on some samples ultracentrifugally at a density of 1.063 by the method of Gofman and associates[2] or at a density of 1.21 by the method of Lewis and associates.[3]

Results

The serum cholesterol concentration immediately after and a short time after smoking was essentially unchanged in most subjects (table 1). There seemed to be no greater variations in the subjects who were habitual smokers than in the nonsmok-

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From the Research Division of the Cleveland Clinic Foundation and the Frank E. Bunts Educational Institute.

ers. In one man, subject 1, there was a decrease, apparently as a result of smoking. The cause for this is not found. Subject 12, who was studied after smoking on the same day as subject 1, showed a slight, but not significant, decrease one-half hour after 10 minutes of deep breathing.

There was no significant change after smoking in the serum lipoprotein pattern of the 10 subjects for whom the lipoprotein levels were measured, at densities 1.063 and 1.21. The lipoprotein results (table 2) serve to show the good reproducibility of the method; the patterns looked like duplicates of the same sample.

Small variations in the total cholesterol concentration were accompanied by similar small changes in total protein level, suggesting that they were probably due to slight fluid shifts.

Comment

The results reflect the relatively stable level of the serum cholesterol and lipoprotein levels for short periods. The slight stress of blood drawing or smoking was not sufficient to modify them.

The lack of effect of smoking on the cholesterol and lipoprotein levels in the nonsmoking persons was striking. They had smoked two cigarettes with inhaling, and this could be considered to be a not inconsiderable stress. At the end of the smoking both subjects felt dizzy and chilly but no change was observed.

We know little of the long-time effect of smoking on the serum cholesterol or lipoprotein levels. Changes in eating habits resulting from smoking could play an important part in varying the cholesterol concentration.

In a study of serum lipoprotein and cholesterol levels in smokers as compared with nonsmokers, Gofman and associates[4] observed a *significantly* higher concentration in men aged 20-29 years who smoked. The differences were not significant in the older age group of either men or women. In our studies there was no difference between the results on young or older subjects or between the sexes.

TABLE 2.—*Serum Lipoprotein Levels Determined at Two Densities Before and After Smoking*

Subject No.	Sample No.*	Total Protein Level, Gm./100 Ml.	Cholesterol Level, Mg./100 Ml.	Lipoprotein Level, Mg./100 Ml. -S70-400‡	40-70‡	25-40‡	20-25‡	1-10‡	S_f12-20§	S_f20-100§
11	A	...	256	90	71	390	14	212	..	..
	B	...	258	71	71	376	14	225	..	..
	C	...	258	71	60	390	19	212	..	..
	D	...	261	38	71	430	14	230	..	..
13	A	7.35	228	38	56	260	19	333	..	..
	B	7.60	224	33	52	280	19	345	..	..
	C	7.50	227	28	56	285	23	336	..	..
	D	7.50	231	33	52	290	19	348	..	..
14	A	7.60	227	52	71	400	23	225	78	26
	B	7.60	224	47	71	400	23	243	87	22
	C	7.55	218	42	66	400	33	207	70	30
	D	7.60	218	52	52	376	23	216	65	34
15	A	7.00	251	28	71	390	19	320	69	52
	B	7.00	251	33	66	376	19	330	65	47
	C	6 75	241	38	71	420	14	276	69	47
	D	7.00	248	19	66	400	19	295	61	43
16	A	...	176	23	35	260	19	322	..	..
	B	...	170	26	30	260	16	340	..	..
17	A	6.80	204	19	33	260	28	244	14	18
	B	6.68	189	14	28	240	28	255	14	11
	C	6.48	190	19	24	240	23	260	14	18
	D	6.48	181	19	28	250	28	244	..	..
18	A	6.95	273	49	66	450	21	380	70	53
	B	7.12	278	†	†	†	†	†	70	58
	C	6.70	271	38	66	400	24	345	60	72
	D	6.75	278	42	61	420	21	345	65	53
19	A	6.52	210	24	73	255	14	258	..	..
	B	6.65	207	35	77	265	14	280	..	..
	C	6.60	198	35	71	276	14	276	..	..
	D	6.65	211	42	75	260	14	299	..	..
20	A	7.05	194	9	45	270	19	255	..	..
	B	7.10	198	9	33	285	23	225	..	..
	C	7.00	190	0	33	300	23	239	..	..
	D	7.00	188	0	37	280	19	243	..	..
2B	A	...	172	0	19	174	19	322	..	..
	B	...	167	0	14	160	19	310	..	..
	C	...	165	0	19	180	14	300	..	..
	D	...	162	0	14	174	14	310	..	..

* Sample A = presmoking "control"; B = end of smoking; C = 10 minutes after end of smoking; and D = 30 minutes after end of smoking.

† Lost in preparation.

‡ Determined at density 1.21.

§ Determined at density 1.063.

Summary

The rapid smoking of two nonfilter-tip cigarettes by habitual smokers or nonsmokers was without effect in modifying serum cholesterol or lipoprotein concentrations during the 30-minute period immediately after smoking. If this form of smoking *is a stress, it is insufficient* to change blood cholesterol or lipoprotein levels during short periods of time. Over short periods of time the cholesterol and lipoprotein levels are constant.

2020 E. 93rd St. (6) (Dr. Page).

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TREATMENT OF POSTALCOHOLIC SYNDROME WITH TRIFLUPROMAZINE HYDROCHLORIDE

Harold I. Goldman, M.D., Denver, Colo.

The acute alcoholic inmate of a county or city prison presents special problems of management. The boisterousness, hallucinosis, nausea, tremors, and involuntary defecation and urination, which characterize the postalcoholic state, are not only distressing to the prisoner but also add to the general disturbance of the prison population and increase the burden of custodial care. To alleviate these problems, a simple regimen, effective in controlling withdrawal symptoms in the alcoholic prisoner, is desirable.

In recent years, a number of the so-called tranquilizing drugs have been employed in the treatment of the alcoholic patient. Some of the most effective of these drugs in treatment of patients in the postalcoholic state have been the phenothiazine derivatives.[1] Recently a new phenothiazine compound, triflupromazine hydrochloride, has been made available for trial in controlling symptoms of alcohol withdrawal.

For about a year, triflupromazine, supplied as Vesprin, has been under study at the Denver city jail, to evaluate its effectiveness in treating alcoholic prisoners. Up to the present time a total of 252 prisoners have been treated with triflupromazine hydrochloride. From the results obtained, it would appear that this substance is a valuable adjunct in the treatment of the postalcoholic syndrome. Results of this study are briefly reported.

Methods and Materials

Patients.—The series comprised a total of 252 subjects. Of these, 221 were men, and 31 were women. All were intoxicated on admission, but none had acute delirium. None of the prisoners was addicted to narcotics. The symptoms of alcohol withdrawal which were observed during this study included boisterousness, tremors, hallucinosis, and nausea. Police officers were provided with check sheets on which to record their observations of the patients (table 1). Representative blood pressure readings were taken at random among the prisoners to serve as "spot checks" for any hypotensive response to the drug. Instructions were given to record any other undesirable reactions to the drug.

Table 1.—*Check Sheet Used by Police Officers to Record Effects of Triflupromazine on Prisoners*

This drug is to be used in the city jail experimentally and the results observed and reported to Dr. Goldman. The dosage is one (1) tablet which may be followed with another every four (4) hours, if necessary. It is to be used for the shakes and other postalcoholic reactions.

Fill in the 1st and 2nd lines at the time the drug is given.

After observing the prisoner for one hour or more the report may be completed and filed in the medicine box.

1. Prisoner's name ....
2. Date and time given ....
3. Time of observation ....
4. Did the prisoner's nausea seem to improve? Yes No
5. Did the prisoner's shakes seem to improve? Yes No
6. Was the prisoner able to go to court or be released? Yes No
7. Did the prisoner seem to improve?
8. Officer's name ....

Medication.—Triflupromazine was administered orally in doses of 25 mg. every four hours until the described symptoms disappeared or became

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Police Department, City and County of Denver.

worse (indicating that the drug was ineffective in these cases). In cases in which there was no apparent response to the drug, the dosage was increased so that at least four doses (25 mg. each) were given within 6 to 12 hours. Total daily doses ranged from 150 to 400 mg.

Results

In 212 of the 252 patients treated with triflupromazine, at least two of the observed symptoms improved (table 2). Sixteen patients required treatment for 24 hours or longer before any improvement was apparent. Forty patients showed no improvement at any time (or their symptoms became worse) after administration of triflupromazine. All of those who responded to triflupromazine markedly improved in their boisterousness and hallucinations. The drug failed to control nausea in 43 subjects or tremors in 49. Of the 221 men treated, 182 (82.4%) improved and 39 did not. Of the 31 women treated, 30 (96.8%) improved and only one did not. No significant changes in blood-pressure were observed in the "spot check" readings made after administration of triflupromazine. No other undesirable reactions to the drug were recorded.

TABLE 2.—*Effectiveness of Triflupromazine Hydrochloride in Controlling Symptoms in 252 Patients During Alcohol Withdrawal*

	Patients		
Symptoms Evaluated	Improved, No.	Unimproved, No.	% Improved
Boisterousness	212	40	84.2
Tremors	203	49	80.6
Hallucinosis	212	40	84.2
Nausea	209	43	82.9

Comment

The results of this study support the observations of others[2] that triflupromazine is useful in controlling symptoms of alcohol withdrawal. The effectiveness of the drug in controlling the boisterousness and hallucinosis in the majority of alcoholic prisoners under treatment was a definite contribution to an increased equanimity and easier management of the prison population. The period of therapy was too short to permit critical evaluation of undesirable side-effects or allergic reactions to the drug; but the fact that no significant hypotensive or other side-effects were observed indicates that, in the doses given, side-effects would present little, if any, difficulty.

The greater effectiveness of triflupromazine in women than in men may have clinical significance. A better level of improvement in behavior has also been reported in female than in male schizophrenic patients during treatment with triflupromazine.[3] Further studies to ascertain whether a difference exists in the response of the different sexes to this therapy would be of clinical interest.

Summary

A total of 252 alcoholic prisoners was treated with triflupromazine (Vesprin) hydrochloride to control the acute symptoms of alcohol withdrawal. This drug was administered orally in doses of 25 mg. every four hours for total doses ranging from 150 to 400 mg. daily. In 212 of the 252 patients, or 84.2%, improvement was observed. By controlling the boisterousness and hallucinosis in these patients, treatment with triflupromazine particularly helped to facilitate custodial care of these prisoners. It would appear that this is a valuable adjunct in the treatment of the postalcoholic syndrome.

1245 E. Colfax Ave. (18).

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THE NORMAL ABDOMEN IN YOUNG PEOPLE.—To determine which abdominal organs are palpable in normal people, the abdomens of 100 healthy male medical students and 100 female student nurses (18-24 years of age) were examined: The descending colon and caecum were felt in most subjects. The wall of the abdominal aorta was felt in most females, but in only about half the males. The liver was felt in only 11 women and 2 men. The right kidney was felt in 11 women but in none of the men; the reason why it is so rarely palpable is the thickness and resistance of the soft tissues and not its position. Other abdominal organs are not normally palpable.—J. G. Bearn, M.B., and T.R.E. Pilkington, M.D., Organs Palpable in the Normal Adult Abdomen, *Lancet*, Aug. 29, 1959.

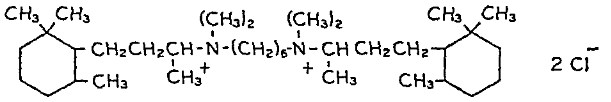
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. KAUTZ, M.D., *Secretary.*

Triclobisonium Chloride (Triburon Chloride).—N,N'-Bis[1-methyl-3-(2,2,6-trimethylcyclohexyl)propyl]-N,N'-dimethyl-1,6-hexanediamine bis(methochloride).—The structural formula of triclobisonium chloride may be represented as follows:



Actions and Uses.—Triclobisonium chloride, a bisquaternary ammonium compound, is an antibacterial agent; applied topically, it is used in the management of superficial skin infections and vaginitis. The organisms most sensitive to its effects, in vitro, are strains of Staphylococcus pyogenes var. aureus, including some that are resistant to commonly employed antibiotics, Streptococcus pyogenes, Diplococcus pneumoniae, Listeria monocytogenes, and Salmonella typhi. In higher concentrations, it inhibits the growth of Pseudomonas aeruginosa, some fungi, and Trichomonas vaginalis. Some strains of Escherichia coli are moderately sensitive, whereas others are almost completely resistant.

Despite its antimicrobial activity in vitro, the efficacy of triclobisonium chloride in the treatment of superficial infections caused by the aforementioned organisms is not clearly established. Early trials have been uncontrolled studies in which no systematic comparison with other quaternary ammonium compounds or with other local anti-infectives, including topically applied antibiotics, was attempted; no double-blind study has been reported. Nevertheless, early clinical reports, especially when the drug was used in the treatment of impetigo contagiosa, are favorable; the drug is said to accelerate recovery in acute folliculitis, furunculosis, infectious eczematoid dermatitis, and other primary pyodermata and secondarily infected dermatoses. It is also reported to be helpful in the management of Trichomonas vaginalis vaginitis, and, to a lesser extent, monilial, and so-called nonspecific vaginitis. Fungus infections of the skin respond poorly. Thus, if subsequent properly designed clinical experimentation substantiates these preliminary impressions, triclobisonium chloride can be regarded as a useful adjunct in the management of superficial infections caused by susceptible organisms.

Topical application of triclobisonium chloride to the skin produces some degree of primary irritation in about 1% of patients; others exhibit signs of sensitization after repeated application. Although, in one study utilizing the closed patch technique, about 2% of normal human subjects developed allergic responses to triclobisonium chloride, fortunately the incidence of such reactions in the clinical use of the drug has been somewhat lower. Experimental instillation of a 1% solution into the eye of the rabbit provoked a slight erythema which subsided within 48 hours and left no residual damage; 0.1% solutions produced no irritation. Ointments and solutions of triclobisonium chloride produced no untoward effect when applied to the vagina of the rabbit. Local application of the drug has not produced toxic effects attributable to systemic absorption either in man or in experimental animals.

See also the general statement on cationic agents in the section on disinfectants and antiseptics in New and Nonofficial Drugs.

Dosage.—Triclobisonium chloride is applied topically or intravaginally. For the treatment of pyogenic diseases of the skin, a cream or ointment containing 0.1% triclobisonium chloride is applied to the affected area three or four times daily and is rubbed in gently. If the drug is applied to extensive or acutely inflamed areas, the patient should be carefully observed for evidence of systemic toxicity, even though such effects have not yet been reported. Because of the occurrence of primary irritation and allergic reactions in some patients, unsupervised use of the drug is not recommended. For the treatment of vaginitis, a single application of triclobisonium cream (0.1%) is introduced into the vagina each night.

Preparations.—cream (topical, vaginal) 0.1%; ointment (topical) 0.1%.

Year of introduction: 1959.

Hoffmann-LaRoche, Inc., cooperated by furnishing scientific data to aid in the evaluation of triclobisonium chloride.

Additional Uses of Chloroquine (Aralen) Phosphate

The Council has reviewed the available evidence concerning the use of chloroquine phosphate in the treatment of lupus erythematosus and rheumatoid arthritis. The use of the drug in the treatment of malaria and systemic amebiasis is currently described in New and Nonofficial Drugs.

The value of chloroquine phosphate in chronic discoid lupus erythematosus is now generally accepted. It appears to be equally as effective as quinacrine and considerably less toxic. About 60% of patients exhibit complete remission or marked improvement characterized by regression of skin lesions and increased tolerance to light. Progress is most rapid during the first month of treatment but may continue at a more gradual rate for several weeks thereafter. About one-third of the patients who respond relapse when administration of chloroquine phosphate is discontinued, but many of these will again respond to readministration of the drug.

The status of chloroquine phosphate in the disseminated or systemic form of lupus erythematosus is controversial. The drug must not be relied upon in the acute form of the disease. In the subacute and chronic phases, some investigators have reported favorable results, whereas others have expressed the opinion that the drug aggravates the symptoms and is contraindicated. Large doses are said to be especially likely to cause a flare-up of constitutional symptoms. The administration of small doses of chloroquine phosphate to patients receiving adrenocorticosteroids has been reported to produce favorable results and to make possible a reduction in dosage of the steroids.

Chloroquine phosphate frequently produces some symptomatic relief in rheumatoid arthritis and thus may be a useful supplement to the basic therapeutic regimen of rest, physiotherapy, and diet.

In this condition the response is typically delayed; although subjective relief may be reported within 2 weeks after administration is begun, objective signs of improvement are ordinarily visible only after 6 weeks to 3 months, and maximum benefit only after 6 to 12 months. Any improvement produced is generally maintained with continued treatment, although many patients continue to exhibit minor exacerbations and remissions. As might be expected, patients with gross joint damage respond poorly; otherwise there is little correlation between the degree of response and the duration and stage of the disease or the severity of the inflammatory process. The sedimentation rate, erythrocyte count, and other laboratory findings may show a little change, even in the presence of clinical improvement. Chloroquine phosphate may be used in conjunction with salicylates, and, when so used, a reduction in dosage of the latter drugs is often possible. Combinations of chloroquine phosphate and adrenocorticosteroids, gold salts, and other antirheumatoid drugs have had only limited trial; the value and possible dangers of such combinations are unknown, but it would seem that drugs with similar side-effects, such as rashes, should be avoided. Patients who have relapsed while on steroid therapy rarely respond to administration of chloroquine phosphate.

The mechanism of action of chloroquine phosphate in lupus erythematosus and rheumatoid arthritis is unknown. It has been suggested, however, that these and other collagen diseases represent hypersensitivity reactions and that chloroquine phosphate suppresses the formation of the antigens responsible for the reactions, whereas adrenocorticosteroids interfere with the reaction after it is established.

Although chloroquine phosphate is well tolerated as used in the treatment of malaria, side-effects occur frequently and are often of considerable severity when it is employed for the treatment of lupus erythematosus or rheumatoid arthritis. About 10% of patients with these diseases are unable to tolerate adequate doses. The percentage of patients to whom the drug is acceptable can be increased by starting with very small doses and gradually increasing this dosage. Among the less serious reactions reported are headache, pruritus, visual disturbances, gastrointestinal complaints, and lymphedema of the forearm and hands. Skin reactions occur frequently and include dryness, itching, urticaria, maculopapular eruption, desquamation, exfoliation, increased pigmentation, alopecia, and graying or bleaching of the hair; preexisting psoriasis may become worse. Exposure to the sun or to ultraviolet may severely aggravate the dermatitis. The more severe skin reactions often necessitate withdrawal of the drug. Leukopenia, which has been reported, also requires that administration of the drug be stopped. Temporary blurring of vision due to interference with accommodation has been observed. Corneal changes, such as edema or opacification of corneal epithelium, with or without such symptoms as visual halos or blurred vision, have been noted on slit-lamp examinations. These changes, which may begin several weeks to several years after treatment is begun, are thought to be reversible. Should such changes occur, however, the advantages of discontinuing the drug must be weighed, in each case, against the therapeutic benefits that may accrue from continuation of treatment. Gastrointestinal intolerance, dizziness, and headaches also occur.

All patients receiving chloroquine phosphate should have periodic blood cell counts.

The dose of chloroquine phosphate in chronic discoid lupus erythematosus is 250 mg. per day, administered orally. Treatment may be continued until maximum benefit is obtained. Should relapse occur after the drug is withdrawn, it may again be administered at the same dosage level.

If chloroquine phosphate is tried in disseminated lupus erythematosus, the initial doses should be very small: 25 to 50 mg. given on alternate days. The dosage may be gradually increased in accordance with the patient's tolerance. The use of larger doses initially may precipitate an acute exacerbation of an already critically severe illness.

In the treatment of rheumatoid arthritis, 250 mg. is administered daily as a single oral dose. If no beneficial effects are apparent after 6 to 12 weeks of treatment, it is unlikely that continued administration of the drug will result in improvement, though maximum response may be delayed for six months or more.

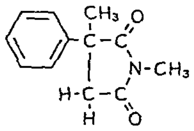
If troublesome minor side-effects appear during the treatment of either rheumatoid arthritis or lupus erythematosus, the drug should be withdrawn for a few days and treatment reinstituted at a reduced dosage level. The dose may then be cautiously and gradually increased as the patient's tolerance permits.

Administration of chloroquine phosphate should be stopped immediately, and should not be resumed, if marked leukopenia or severe skin reactions appear.

The Council voted to amend New and Nonofficial Drugs to describe the use of chloroquine phosphate in the treatment of rheumatoid arthritis and lupus erythematosus.

Winthrop Laboratories cooperated by furnishing scientific data to aid in the evaluation of these additional uses of chloroquine phosphate.

Methsuximide (Celontin).—N,2-Dimethyl-2-phenylsuccinimide.—The structural formula of methsuximide may be represented as follows:



Actions and Uses.—Methsuximide is an anticonvulsant agent closely related chemically and pharmacologically to phensuximide. The two drugs show a similar pattern of activity in suppressing experimentally induced seizures in animals and both are relatively more effective against convulsions induced by pentylenetetrazole than those produced by electroshock.

In the reported clinical trials, methsuximide reduced significantly the incidence of seizures in about 40% of the patients in whom it was used. Approximately 45% of the patients with petit mal seizures, 40% of those with psychomotor attacks, but only 20% of those with grand mal epilepsy responded favorably. It provided complete control of seizures in about 15% of cases of petit mal and 10% of psychomotor attacks.

Approximately 30% of patients receiving methsuximide experience undesirable side-effects. In descending order of recorded frequency these include drowsiness, ataxia or dizziness, gastrointestinal disturbances (including anorexia, nausea, vomiting, constipation, diarrhea), skin eruptions, irritability, psychic disturbances (ranging from slight alterations of mood or personality to occasional acute psychoses), headache, and diplopia or blurring of vision. Fever, hiccough, and severe diaphoresis have been observed in a few patients. In many instances, aside from patients with rash, reduction in dosage results in elimination of the toxic manifestations.

Although it has not been definitely established that methsuximide damages either the kidney or the liver, several reports are suggestive of such damage; therefore, patients receiving the drug should be carefully observed for evidence of renal or hepatic dysfunction. Two patients have developed periorbital edema, associated in one with albuminuria, during methsuximide therapy. Two others have manifested signs suggestive of hepatic dysfunction, including positive cephalin flocculation test, icterus, tenderness in the region of the liver, and spider angiomas. Although examination of the peripheral blood has disclosed no evidence of adverse effects on the hematopoietic tissues, periodic blood studies should be made during therapy.

In chronic toxicity studies in animals, methsuximide was well tolerated; in rats, however, very large doses produced mild to moderate central lobular necrosis and other cytological changes in the liver.

Methsuximide is not the drug of first choice in any of the forms of epilepsy. It may be effective, however, when other drugs fail. It is most apt to be useful in many cases of psychomotor seizures, which are frequently refractory to other drugs. It may also be tried in petit mal seizures when older, conventional drugs are ineffective or are not tolerated by the patient. Methsuximide is of little, if any, value for the control of grand mal seizures. Methsuximide is apparently more effective when used in conjunction with other drugs; there is no contraindication to using it in combination with any of the other anticonvulsants. The most effective combinations, however, remain to be determined.

Dosage.—Methsuximide is administered orally. The optimal dose for controlling seizures must be carefully determined for each individual patient. However, 300 mg. per day is suggested for initiating treatment. Then, if necessary, the dosage may be gradually increased over a period of several weeks, until a total daily dose up to 1.2 Gm. is reached.

Preparations.—capsules 300 mg.

Year of introduction: 1958.

Parke, Davis & Company cooperated by furnishing scientific data to aid in the evaluation of methsuximide.

MEDICAL EDUCATION IN THE UNITED STATES AND CANADA

Fifty-Ninth Annual Report on Medical Education in the United States and Canada by the Council on Medical Education and Hospitals of the American Medical Association

Walter S. Wiggins, M.D., Glen R. Shepherd, M.D., John Hinman, M.D., and Anne Tipner

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ACKNOWLEDGMENT

This represents the 59th Annual Report on Medical Education in the United States and Canada compiled by the Council on Medical Education and Hospitals. This report is concerned primarily with basic medical education and is a part of the Council's response to one of the charges given it many years ago "To make an annual report to the House of Delegates on the existing conditions of medical education in the United States." Other levels of medical education are the subjects of annual Council reports dealing with internships and residencies [1] and postgraduate medical education.[2]

Much of the statistical data presented were derived from medical schools' responses to a questionnaire prepared jointly by the staffs of the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical Colleges. As far as possible, data available through the Association of American Medical Colleges were utilized in place of requesting similar information directly from the medical schools. Data concerning medical education in Canada were collected through the cooperative efforts of the Association of Canadian Medical Colleges.

The Council on Medical Education and Hospitals is pleased to express appreciation for the American Medical Association to the individual medical schools, the Association of American Medical Colleges and the Association of Canadian Medical Colleges, governmental agencies and other organizations and individuals whose cooperation in furnishing information has made the preparation of this report possible.

NEEDS IN MEDICAL PERSONNEL AND EDUCATIONAL FACILITIES

In recent reports,[3] the Council on Medical Education and Hospitals has indicated sincere concern that there be implemented careful planning directed toward the expansion of educational facilities in medicine. All thoughtful individuals and organizations recognize that a rapidly growing population which becomes ever more health conscious will require a greater number of well qualified physicians as well as other health personnel.

The provision of educational opportunities for the number of medical students adequate to satisfy medical service needs as the general population grows in size is a huge task. To accomplish this task and at the same time maintain high standards of medical education represents a challenge at least as important as any problem facing medicine today.

QUANTITATIVE CONSIDERATIONS

Medical Service Requirements

In general, medical schools have developed to the present in response to local, state or institutional needs and desires. Perhaps fortuitously, the facilities established in this manner have kept pace largely with the immediate service demands of the public and educational desires of young people seeking careers in medicine.

How medical manpower requirements of the future can be met must be dependent initially on reaching agreement as to the dimensions of the requirement.

The problems related to the provision of adequate medical manpower for the future are becoming increasingly urgent. It appears that the time is at hand for accepting available knowledge as the basis for the best possible working definition of future medical requirements.

Two years ago, the Council's Annual Report on Medical Education [3b] explored some of the complexities of utilizing physician population ratios in projecting medical manpower needs. The 54th Congress on Medical Education and Licensure[4] brought together thoughtful leaders of higher education, business and industry, labor, agriculture, insurance, sociology, political science as well as medical practice and medical education. These representatives of large consumer groups and purveyors and producers of medical education considered together the challenges and future needs in medical service and education. Certain of the opinions generally supported by one of the representative groups at that Congress were:

1. The demand for medical service has been approximately in equilibrium with the supply.
2. The physician-population ratio, although not ideal, does constitute the best measure for planning the future medical care which can be brought to bear on the problem at the present time.
3. Since the level of medical care provided by the existing ratio is reasonably satisfactory, until there is a better measure of future needs, it would be prudent to pursue that ratio in planning for the production of physicians over the next several years.
4. Under no circumstances should any course of action be adopted which would cause a deterioration in the quality of medical education.

The physician-population ratio has remained relatively constant throughout the past forty years. During this same period, there have occurred sweeping changes of social, economic and scientific natures which have exercised important influences on the quality and quantity of physicians' services. Some of these changes have assisted in spreading a physician's services over a wider segment of the population; others have tended to restrict the populace served by the physician. Morbidity and mortality data for this four decade period support the contention that the spreading and restricting factors have balanced one another to a reasonable degree. This has allowed the level of medical care to advance grossly, though perhaps not ideally, with advances in medical science.

Therefore, it appears that the best available knowledge for projecting future medical manpower needs is on the basis of the existing physician-population ratio. In utilizing this base, its defects should be acknowledged so that projected figures are recognized as estimated and not endowed with a finiteness which they do not possess.

There have been several recent studies[5] which have projected medical manpower needs on this basis. Although the resulting estimates have differed in degree, they all indicate clearly that there will be required a significant increase in the number of physicians graduated to maintain the present ratio. The projected increment for 1975 over present numbers of medical graduates range from 2,000 to 3,500. In general, the smaller estimates were made earlier when population projections were at a lower level. However, the highest estimate[5d] includes factors other than the simple linear relationship between the anticipated population growth and the number of medical school graduates.

It is expected that in 1960 there will be approximately 7,000 graduates of U. S. medical schools. In view of the estimates referred to above, should the goal for 1975 be 9,000 or 10,500 annual graduates? Because of the potential for error inherent in estimates of this nature which can be significantly altered by many factors—particularly economic ones with their inevitable effect on birth rates—it would seem reasonable to accept as the present goal for 1975, the need for 10,000 graduates from our medical schools.

Educational Facility Requirements

It is important to recall that the general population whose medical service needs must be satisfied will not suddenly change between 1974 and 1975. The population growth will occur on a daily, monthly and annual basis gradually and persistently increasing to the projected total of 235 million by 1975. Similarly, the expansion in educational facilities in medicine should take place gradually and persistently. This will allow for periodic adjustment of the goal of 10,000 graduates by 1975 in keeping with any gross changes in population projections that occur.

The fundamental issue does not involve the question of which of the various studies have resulted in the most accurate estimate of the need for increased numbers of medical school graduates. *The basic and urgent concern is that all estimates indicate a need for expansion of educational facilities in medicine in a brief period which far exceeds any expansion of such facilities that has occurred in a similar period during modern times.*

There are three methods which can be used to meet the need for expanded educational facilities in medicine. They are (1) expanding the capacity of existing medical schools, (2) the development of new medical schools, and (3) the combined expansion of existing schools and the creation of new ones.

Increasing the capacity of existing medical schools would be least costly in terms of capital expenditures and operating costs. Medical schools now functioning have indicated that if funds were available for the necessary construction, it would be possible for them to increase their enrollment by approximately 1,000 students.

Increasing enrollment through this method has the additional advantage of being capable of attainment in a reasonably short period of time. It can be hoped that this approach will satisfy largely the increased needs of the most immediate future. Care must be exercised that medical schools not be induced to expand beyond their capacity to maintain the proportionately increased teaching staff necessary to preserve high standards of education and research.

Because of a justifiable concern with long range financing, several schools were hesitant to indicate the possibility of more than a very modest expansion.

There is a general agreement that the total predicted need for additional graduates cannot be met through adjustments in enrollment of present schools. New medical schools will have to be developed even though existing schools expand. It appears likely that at least ten new schools with an average graduating class of 100 students will be required. At the moment it does not appear urgent that a firm decision be made as to the total number of new institutions that must be established. It is clear that planning for the construction of five additional institutions could be implemented in the very near future without any concern that this number would saturate the need. No parent university will undertake the large expense of a medical school development unless it is convinced that it is necessary. Because of the considerable period required for the study and planning of a medical school's establishment, there will be ample opportunity to re-evaluate future needs so there should be no concern that there will be any overdevelopment.

The present and urgent concern is that there is little secure evidence that the most conservative estimates of medical manpower requirements of the immediate future will be met. The University of Kentucky Medical Center in Lexington is under construction and will admit its first medical school class in September, 1960. The state legislature in Texas has passed enabling legislation for the construction of a third University of Texas Medical School in San Antonio. The University Regents are in the process of site selection and planning but there have been no funds appropriated for capital or operating expenses. Although other institutions and organizations have expressed interest in such a development, there are no other firm commitments.

The Council on Medical Education and Hospitals and the Association of American Medical Colleges have published statements encouraging universities to consider the establishment of two year schools of basic medical sciences. Present medical schools have indicated that their clinical facilities would enable them to accept up to 700 graduates of two year schools into the third year class. Schools of basic medical sciences now functioning have established an effective role for such schools. If others are developed, it is likely that over a period of time some of them would expand to the full four year program. In this instance, it is again important to recognize the inappropriateness of concern with the numbers of basic science schools to be developed until there is some evidence that accepted needs are likely to be satisfied.

The combined approach of expansion of existing schools and development of new schools should prove least costly; it should produce the increasing number of physicians in the gradual manner in which they will be required and at the same time make allowance for geographically orienting new medical schools to population movement.

QUALITATIVE CONSIDERATIONS

The present concern for producing an adequate number of medical school graduates in the future must not overshadow a persisting and concentrated effort to improve the effectiveness of medical education, research and service. As planning for expanded educational facilities take place, present high standards must be maintained in proportion to advances in knowledge.

Medical Students

In the production of capable physicians for careers in medical practice, teaching and research, the single most important element is the quality of the student. A competent and dedicated faculty and a fine physical plant can assure that the student will perform at the highest level of which he is capable. It is very important that faculty and facilities provide the most productive and challenging environment for the student's learning. It is equally important to recognize that the student's inherent ability is the ultimate determinant of his performance. He cannot be raised above himself.

There exists today a widespread interest in all areas of science to attract students of superior ability. In an address before the Federation of State Medical Boards at the 55th Annual Congress on Medical Education and Licensure, Cooper[6] expressed medicine's dilemma, ". . . the increasing mass of scientific knowledge in medicine, the medical sciences, and the behavioral sciences and the deepening complexity of medical practice call out for students with ever greater intellectual capacity and dedication than in the past. If students are not equal to this heavier burden, there can only be compromise with the high level of education necessary to prepare them for the profession. . . . Medicine is finding increased competition for the pool of top-ranking students because it no longer occupies the unique position as a profession which it held in the past and shared largely only with law and the ministry. The professions open to the college graduate are now much broader, and they provide the prestige, intellectual satisfaction, and financial rewards comparable to those offered by medicine. . . . The vast sums of money available for fellowships and research assistantships in the expanding research budgets almost guarantee the total expenses of graduate education for all but a small fraction of students in the physical, biological, and behavioral sciences. Medicine has no equivalent source of subsidy for its students."

While there is as yet no certain documentation that medicine is not attracting its share of well qualified college students, it is evident that the exciting career possibilities in other sciences have captured the imagination of the public at large. Medicine must make active efforts to inform young people of the breadth of interests and challenges it offers or surely it will suffer a serious loss of the best young talent. Through the joint endeavors of the American Medical Association and the Association of American Medical Colleges, informative career information has been developed in interesting form for high school students. Medical teachers and practitioners should take advantage of every opportunity to present this information to young people.

The high birth rates of the early years of World War II are just now being reflected in college enrollments. There will be a large potential pool from which an adequate number of students well qualified for medical careers can be obtained if effort is made. This is a challenge to all of medicine.

Medical School Faculties

The preservation of high standards while expanding educational opportunities in medicine will require a proportionate expansion in teaching personnel. Elsewhere in this report are presented data pertinent to the number of existing faculty vacancies. While this is a substantial number, it has not increased proportionately as much in the past year as in previous years. Somewhat conflicting data regarding the opportunities, enrollments and graduates in the graduate degree program of the medical sciences are also presented. The expanding graduate degree and post doctoral fellowship programs give some assurance that there is a sufficient pool of potential teachers. However, there is a real need for an over-all evaluation of the size and character of this pool.

Research training and experience and research productivity is now most often the basis for full-time academic appointment on medical faculties.

Under appropriate conditions this system has much to commend it. The advancement of knowledge is one of the obligations of any institution of higher education and the imaginative curiosity that should characterize the investigator is an equally highly valued trait for a teacher. However, there may be reason to question the extent to which appropriate conditions do exist today.

Many individuals have expressed concern that the broad impact of the widespread project type research grant in the long view may not be beneficial to research itself or to the individual and educational institution involved. This concern is reflected in the recommendations of a recent NIH staff committee study.[7]

Commenting on this issue, Dr. Long[8] stated, ". . . there has been brought into science departments a large number of individuals for whom the university has no direct responsibility. . . . Since research under the terms of the grant must command their first loyalty, how can we expect them to participate in other educational activities of the department. . . . Two or three years postgraduate fellowship experience is essential for development of an independent investigator, but the emergence of a group of journeymen scientists does not seem . . . to be a happy consequence of our present system. . . .

". . . the medical schools and all branches of the university require not only investigators in their particular field, but also individuals who are capable of teaching the next generation. The present emphasis on research as the most important criteria for advancement, with the consequent development of a highly competitive character to research, has tended to obscure the importance of the teacher in the future of medical science. It would be well to remember that *research is a component of good teaching. . . .*" (emphasis supplied).

In the development and acquisition of full-time faculty for the expanded educational facilities, Dr. Long's comments should be given deliberate thought.

Medical School Curriculum

Expansion of the physical plant of medical education should be preceded by a careful study of the kind of an educational program the plant should house. During the past decade, many medical schools have reviewed their curricula and several institutions have established standing faculty committees charged with this as a continuing responsibility. In schools recently developed as well as in others long established, the unit student laboratory concept has gained wide acceptance. In at least two new schools, there have been included physical facilities for patients admitted for diagnostic work-up or patients in a convalescent stage, who require less than the usual full hospital care and more than the usual out-patient services.

These latter facilities should be conducive to approaching medicine as a study of the interaction of man and his environment in which medicine inevitably must draw to a greater extent on the social sciences as knowledge in these disciplines becomes more secure. The social implications of health and disease and, to the usual physician teacher or practitioner, the more immediately important implications of social components as either direct or contributory factors in health and disease are generally recognized and accepted. Though medical teaching now borrows from the social sciences, there is still much fumbling. Perhaps the major problem centers about the inability to bring social concepts into medical education as a viewpoint incorporated as a part of the attitude and philosophy of all medical teachers. As this evolves, it is likely that there will be a greater scientific base to what is now known as the art of medicine.

Medicine becomes more and more truly scientific as it relates the advancing knowledge of the fundamental sciences to biology. The rapid developments, particularly in nuclear physics and atomic energy, present impressive challenges to medicine and its related sciences. In order for medicine to capture all possible benefits from these areas of science, there must be available as teachers, researchers and students, individuals with a depth of knowledge in modern physics and chemistry and an interest and ability in relating new discoveries to medical ends. This whole area will surely have an increasing importance to and a greater role in medical education.

Many occurrences make it clear that the physician and medical teacher of tomorrow must be in his intellectual and clinical activities far more knowledgeable in the basic sciences and intimate with the laboratory and sociological areas. The background for this closer identification is already being acquired by increasingly large numbers of medical students who actively participate in research during the summer vacation period or during free or elective hours of the regular academic year.

The construction of new facilities should take these and other similar matters into account.

NEW DEVELOPMENTS IN MEDICAL SCHOOLS

Sixty medical schools in the United States and eight of the Canadian institutions reported developments of major interest during the past year. These developments are in such areas as administrative organization, curriculum planning and activation, and augmented financial resources. Readjustments in financing covered funds for salary increases for the faculty, for maintenance and operation, new equipment, construction, increased resources for student loans and scholarships, changes in methods of selection of students, and additions to endowment resources.

Thirty-one schools in the United States and two in Canada reported changes of *administrative* organization. These vary from changes of key administrative personnel to major readjustments of departmental interrelationship. A student sponsor program has been initiated at George Washington University. Senior members of the faculty assume sponsorship of four students, one from each class. The students call on their advisor for help with various problems. The University of Miami has established a Medical School Council to develop contacts with representatives of the general public in a more intimate and active manner than is usual in a routine public relations program. The Council was organized to include 21 business and professional men of the community. Its organization includes four committees—public relations, long range development, finance, and physicians.

Vanderbilt University, with a grant from the Commonwealth Fund, has embarked on a study to evaluate the present status of the medical center and to formulate its goals for the future. The faculty has been engrossed in this study throughout the year. A pattern of close administrative coordination between the Texas Medical Center and Baylor University College of Medicine was accomplished during 1958-1959. Under this new arrangement, general policies for the medical school are developed by a Joint Administrative Committee, composed of three representatives from the Board of Trustees of the University, three from the Board of Directors of the Texas Medical Center, and a seventh public member. In effect, this has added four prominent citizens to the group which now most actively supervises the activities of the College of Medicine. Up to the present time, the Committee has concerned itself largely with matters having to do with financial support and establishment of affiliation arrangements.

A significant move has been the setting up of a Medical Center Planning Committee by the University of Saskatchewan. The new committee is made up of representatives of the Board of Governors of the University, the University Hospital Board, and the Department of Public Health of the Government of Saskatchewan. It has set for itself the task of redefining the goals of the medical center.

The Yale–New Haven Medical Center has been incorporated for the purpose of joint action of the Yale School of Medicine and the Grace–New Haven Community Hospital in those areas of the activities of the two institutions where there are mutual interests, such as public relations, long-term planning, and fund-raising. The university and the hospital will continue to be independent corporate entities and the university will continue to be responsible for teaching and research and the hospital for service. Funds received by the medical center will be distributed to the two institutions for the purposes stated and in accordance with the interests of the donors.

Through the efforts of the medical school administration, the Rockefeller Foundation allocated $50,000 to Boston University to design a curriculum suitable for the education of the doctor of tomorrow. This would include the courses that are now required for premedical as well as medical education. The so-called Rockefeller Plan has as its objective to combine the liberal arts and the medical programs of study into a single integrated unit extending over a six-year period, the improvement of the scientific background of the student, to strengthen the educational background of the medical student in the arts and humanities, the development of a scholarly mind, to improve the physician's understanding of the relationship of medicine to society and the duties of a doctor as a citizen, and to make him desire to assume the associated obligations and to increase the sense of responsibility of the doctor toward his patients, other doctors, and the various people with whom he works.

Fifteen medical schools in the United States and one in Canada indicated changes in procedures of *student selection*. The University of Miami, which has previously required a seven-year residence in Florida for admission to its classes, will admit students if they have legal residence in the state. This period has been set at one year by the state legislature. By the terms of the subsidy granted to the school by the state, 90% of the student body must be residents of the state. The definition of residence has been modified so that the medical school admission requirement is now the same as for other educational institutions operated by the state.

The faculty at the University of Chicago in the spring of 1959 recommended a change in the admissions requirements, as a result of which there will be a reduction in both the biology and chemistry requirements of applicants for admission in 1960 and thereafter. In particular, an applicant will not be required to have comparative anatomy, embryology, or qualitative chemical analysis to qualify for admission to the medical school beginning in 1960. The purpose of these changes in the admission requirements is not to reduce the science background of the medical applicants but rather to make the premedical science requirements less rigid so that prospective medical students can pursue a broader and more flexible program of studies in preparing for admission to medical school.

At the beginning of the school year, the first year class of medical students at the University of Washington was given tests for vocabulary and reading speed and comprehension. Those students scoring lowest in the test were given an opportunity to take a remedial course which was financed by the School of Medicine and given with the cooperation of the College of Education of the University of Washington. A faculty committee of the University of Wisconsin has been dealing with the problem of improving methods of selecting and recruiting medical students. The committee has been active across the state in presenting programs for prospective students, parents, teachers, and advisors. In addition, similar programs have been presented in the medical center to acquaint these groups with the medical school's aims, needs and procedures.

There continues to be deep interest in *curriculum* modifications in keeping with the changing emphases on various aspects of medical education. The following material has been selected from the annual reports as illustrative of the dynamic thinking and action generally apparent in medical schools.

During the past two years, the entire curriculum of the medical school of Georgetown University has been restudied and replanned. In particular, the teaching activities of the first two years have been strongly coordinated and the didactic portion of the program in the third year no longer has departmental identification. The teaching in that year is done by means of interdepartmental conferences and panels. New courses have been introduced in growth and development and mechanisms of disease.

With construction of a new basic science building in Indianapolis, the first-year teaching program of Indiana University School of Medicine was moved from the main University Campus in Bloomington to Indianapolis. Beginning in September, 1959, the Indiana University initiated a new program in medical education utilizing the vacated facilities on the Bloomington campus as well as the teaching facilities of other departments of the university. This new venture is designed to permit carefully selected students to complete the first two years of medical study while at the same time continuing work in an academic field through the baccalaureate and master degree levels.

Since January, 1958, the chairman of the department of radiology of the University of Louisville has been on leave of absence to devote his full time to curriculum planning. Implementation of the changes proposed is contemplated in the near future. One of the changes proposed is to reduce the time allotted to the clinical clerkships in the senior year and to substitute for it more work of a purely academic nature in the realm of the humanities as well as in the more strictly scientific areas.

The Wayne State University College of Medicine, in cooperation with other colleges of the university, is embarking on two new programs of instruction which will require drastic alteration of their admission procedures. The first change will be necessitated by the adoption of the 2-4-2 plan of medical college organization. This plan, beginning with two years of liberal arts education, followed by four years of a joint curriculum including both liberal arts subjects and the basic sciences, and concluding with the two clinical years, will likely start next year. The second new program will result from the creation of a "general college" at the University organized around three synthesized areas—the natural sciences, the social sciences, and the humanities. This college, known as Monteith College, enrolled its first group in 1959, and the College of Medicine will tentatively commit 25 places in the first year class of 1963 to students at the time of their entry into the general college. These admissions are provisional and may be cancelled in the event of unsatisfactory collegiate performance. It is the medical college's intention to run these two groups of home-bred admissions alongside the usual out-of-institution and out-of-state groups routinely admitted by the usual procedures.

The State University of New York Downstate Medical Center has planned certain curriculum changes. One-half of a 12-month fourth year will be spent in a comprehensive, nondepartmentalized, combined inpatient and outpatient clerkship. Most of the clerkships in the third year will be given in the Kings County Hospital. The remaining clerkships in both the third and fourth years will be given in the voluntary affiliated hospitals of Brooklyn.

Study of the curriculum at the University of Rochester has resulted in a number of changes which will be introduced in 1959-1960. These include an introduction in the first year to the scholarly and social aspects of the physician's role. At the beginning of the third year there will be an introductory clerkship, taught interdepartmentally, in which emphasis will be placed on medical interviewing and physical examination. Instructors will work in pairs with a group of five students. All clinical departments will participate.

MEDICAL SCHOOLS

APPROVED MEDICAL SCHOOLS

Table 1 lists by states the approved four-year medical schools and schools of basic medical sciences, showing for each school public or private ownership, year of organization, tuition charges, enrollment by class, and other basic data. Similar data are presented in the same table for the newly developing schools now provisionally approved on the basis of implementation of the first two years of the program. Table 2 portrays similar data for the 12 approved medical schools in Canada.

In 1958-1959, Albert Einstein College of Medicine graduated its first medical class and became a fully approved four-year school. This increases the

TABLE 1.—*Approved Medical Schools and Schools of the Basic Medical Sciences in the United States*

State	No.		Owner-ship	Year Organ-ized	Tuition		Premedical Require-ment by Year	Students by Classes, 1958-1959 (Full-time, Part-time and Special Students Included)					Grad-uates 7/1/58 to 6/30/59		
					Resident	Non-resident		1st Yr.	2nd Yr.	3rd Yr.	4th Yr.	Total			
Ala.	1	Medical College of Alabama, Birmingham	Pub.	1859	445.00	845.00	3	81	80	71	65	297	61	Robert C. Berson, M.D., Dean	1
Ark.	2	University of Arkansas School of Medicine, Little Rock	Pub.	1879	500.00	1,000.00	3	95	85	89	70	339	69	F. Douglas Lawrason, M.D., Dean	2
Calif.	3	College of Medical Evangelists, Loma Linda, Los Angeles	Pri.	1909	1,250.00	1,250.00	3	114	91	86	80	371	81	Walter E. Macpherson, M.D., Dean	3
	4	University of California School of Medicine, Los Angeles	Pub.	1951	386.00	736.00	3	56	54	51	47	208	46	Stafford L. Warren, M.D., Dean	4
	5	University of Southern California School of Medicine, Los Angeles	Pri.	1885	1,120.00	1,120.00	3	68	62	64	66	260	66	Clayton G. Loosli, M.D., Dean	5
	6	Stanford University School of Medicine, Palo Alto	Pri.	1908	1,005.00	1,005.00	3	61	62	58	56	237	57	Robert H. Alway, M.D., Dean	6
	7	University of California School of Medicine, San Francisco	Pub.	1864	385.00	735.00	3	101	74	83	80	338	80	John B. deC. Saunders, M.D., Dean	7
Colo.	8	University of Colorado School of Medicine, Denver	Pub.	1883	655.00	1,055.00	3	86	76	72	83	317	81	Robert J. Glaser, M.D., Vice President and Dean	8
Conn.	9	Yale University School of Medicine, New Haven	Pri.	1812	1,175.00	1,175.00	3	81	81	75	79	316	79	Vernon W. Lippard, M.D., Dean	9
D.C.	10	Georgetown University School of Medicine, Washington	Pri.	1851	1,260.00	1,260.00	3 or 4	112	96	103	93	404	93	Hugh H. Hussey, M.D., Dean	10
	11	George Washington University School of Medicine, Washington	Pri.	1825	1,000.00	1,000.00	3	101	97	100	91	389	91	John L. Parks, M.D., Dean	11
	12	Howard University College of Medicine, Washington	Pri.	1868	591.75	591.75	3	105	86	69	77	337	75	Robert S. Jason, M.D., Dean	12
Fla.	13	University of Miami School of Medicine, Coral Gables	Pri.	1952	800.00	1,500.00	3	75	73	55	59	262	59	Homer F. Marsh, Ph.D., Dean	13
Ga.	14	Emory University School of Medicine, Emory University	Pri.	1854	1,000.00	1,000.00	3	74	70	71	66	281	65	Arthur P. Richardson, M.D., Dean	14
	15	Medical College of Georgia, Augusta	Pub.	1828	455.00	None	3	102	91	87	90	370	88	Harry B. O'Rear, M.D., Dean	15
Ill.	16	Chicago Medical School	Pri.	1912	1,070.00	1,070.00	4	72	68	67	67	274	68	John J. Sheinin, M.D., President	16
	17	Northwestern University Medical School, Chicago	Pri.	1859	1,050.00	1,050.00	3	132	122	131	136	521	133	Richard H. Young, M.D., Dean	17
	18	Stritch School of Medicine of Loyola University, Chicago	Pri.	1915	950.00	950.00	3	88	80	84	88	340	86	John F. Sheehan, M.D., Dean	18
	19	University of Chicago, The School of Medicine	Pri.	1927	1,060.00	1,060.00	3	73	74	73	70	290	69	Lowell T. Coggeshall, M.D., Dean, Division of Biological Sciences	19
	20	University of Illinois College of Medicine, Chicago	Pub.	1881	343.50	763.50	3	201	180	170	156	707	153	Granville A. Bennett, M.D., Dean	20
Ind.	21	Indiana University School of Medicine, Indianapolis	Pub.	1903	430.00	750.00	3	160	148	138	139	585	140	John D. Van Nuys, M.D., Dean	21
Iowa	22	State University of Iowa College of Medicine, Iowa City	Pub.	1850	400.00	800.00	3	120	110	108	99	437	100	Norman B. Nelson, M.D., Dean	22
Kans.	23	University of Kansas School of Medicine, Lawrence, Kansas City	Pub.	1905	475.00	925.00	4	98	100	102	102	402	101	W. Clarke Wescoe, M.D., Dean	23
Ky.	24	University of Louisville School of Medicine	Pri.	1837	900.00	1,300.00	3	100	92	91	87	370	86	J. Murray Kinsman, M.D., Dean	24
La.	25	Louisiana State University School of Medicine, New Orleans	Pub.	1931	120.00	520.00	3	129	105	99	110	443	110	William W. Frye, M.D., Dean	25
	26	Tulane University School of Medicine, New Orleans	Pri.	1834	1,110.00	1,110.00	3	134	121	120	119	494	118	Maxwell E. Lapham, M.D., Dean	26
Md.	27	Johns Hopkins University School of Medicine, Baltimore	Pri.	1893	1,280.00	1,280.00	Year 1: 2 or 3 Year 2: Degree	74	72	68	68	282	68	Thomas B. Turner, M.D., Dean	27
	28	University of Maryland School of Medicine & College of Physicians and Surgeons, Baltimore	Pub.	1807	786.00	936.00	3	100	95	85	83	363	83	William S. Stone, M.D., Dean	28
Mass.	29	Boston University School of Medicine	Pri.	1873	1,200.00	1,200.00	4	74	71	75	65	285	66	Chester S. Keefer, M.D., Dean	29
	30	Harvard Medical School, Boston	Pri.	1783	1,068.00	1,068.00	2	114	110	144	148	516	147	George Packer Berry, M.D., Dean	30
	31	Tufts University School of Medicine, Boston	Pri.	1893	1,215.00	1,215.00	3	114	110	104	104	432	104	Joseph M. Hayman Jr., M.D., Dean	31
Mich.	32	University of Michigan Medical School, Ann Arbor	Pub.	1850	550.00	980.00	3	197	180	178	189	744	186	William N. Hubbard, M.D., Dean	32
	33	Wayne State University College of Medicine, Detroit	Pub.	1885	552.00	981.00	3	125	73	64	66	328	66	Gordon H. Scott, Ph.D., Dean	33
Minn.	34	University of Minnesota Medical School, Minneapolis	Pub.	1883	505.00	915.00	3	139	123	126	116	504	113	Robert B. Howard, M.D., Dean	34
Miss.	35	University of Mississippi School of Medicine, Jackson	Pub.	1903	600.00	825.00	3	78	68	64	62	272	62	David S. Pankratz, M.D., Dean	35
Mo.	36	University of Missouri School of Medicine, Columbia	Pub.	1840	355.00 to 498.00	None	3	76	69	59	30	234	31	Vernon E. Wilson, M.D., Dean	36
	37	Saint Louis University School of Medicine	Pri.	1903	1,000.00	1,000.00	3	126	109	100	116	451	116	James W. Colbert Jr., M.D., Dean	37
	38	Washington University School of Medicine, St. Louis	Pri.	1899	924.00	924.00	3	86	83	85	88	342	88	Edward W. Dempsey, M.D., Dean	38
Neb.	39	Creighton University School of Medicine, Omaha	Pri.	1892	1,012.00	1,012.00	3	77	64	66	70	277	70	Richard L. Egan, M.D., Dean	39
	40	University of Nebraska College of Medicine, Omaha	Pub.	1881	525.00	765.00	3	81	75	84	72	312	72	James P. Tollman, M.D., Dean	40
N.Y.	41	Albany Medical College of Union University	Pri.	1839	1,012.00	1,012.00	3	65	59	54	51	229	51	Harold C. Wiggers, Ph.D., Dean	41
	42	University of Buffalo School of Medicine	Pri.	1846	1,080.00	1,080.00	3	88	76	66	70	300	70	Ernest Witebsky, M.D., Dean	42
	43	Albert Einstein College of Medicine of Yeshiva University, New York City	Pri.	1955	1,050.00	1,050.00	4	96	95	91	50	332	50	Marcus D. Kogel, M.D., Dean	43
	44	Columbia University College of Physicians and Surgeons, New York City	Pri.	1767	1,183.00	1,183.00	3	120	121	118	118	477	117	H. Houston Merritt, M.D., Dean	44
	45	Cornell University Medical College, New York City	Pri.	1898	1,250.00	1,250.00	4	86	81	88	82	337	82	John E. Dietrick, M.D., Dean	45
	46	New York Medical College, Flower &												Ralph E. Snyder, M.D.,	

	47	New York University College of Medicine, New York City	Pri.	1841	1,217.00	1,217.00	3	132	130	133	131	526	132	Donal Sheehan, M.D., Dean	47
	48	State University of New York, Downstate Medical Center, New York City	Pub.	1860	715.00	715.00	3	154	135	141	140	570	138	Robert A. Moore, M.D., President and Dean	48
	49	University of Rochester School of Medicine and Dentistry	Pri.	1920	1,275.00	1,275.00	3	69	70	60	63	262	63	Donald G. Anderson, M.D., Dean	49
	50	State University of New York, Upstate Medical Center, Syracuse	Pub.	1834	715.00	715.00	3	87	73	75	67	302	65	Carlyle Jacobsen, Ph.D., Dean	50
N.C.	51	University of North Carolina School of Medicine, Chapel Hill	Pub.	1879	671.00	1,271.00	3	70	64	70	60	264	59	W. Reece Berryhill, M.D., Dean	51
	52	Duke University School of Medicine, Durham	Pri.	1930	1,200.00	1,200.00	3	79	75	76	81	311	78	Wilburt C. Davison, M.D., Dean	52
	53	Bowman Gray School of Medicine of Wake Forest College, Winston-Salem	Pri.	1902	900.00	900.00	3	55	53	51	48	207	47	Coy C. Carpenter, M.D., Dean	53
Ohio	54	University of Cincinnati College of Medicine	Pub.	1819	750.00	950.00	3	92	82	89	79	342	79	Stanley E. Dorst, M.D., Dean	54
	55	Western Reserve University School of Medicine, Cleveland	Pri.	1843	1,000.00	1,000.00	3 (4 Preferred)	78	80	88	75	321	72	Douglas D. Bond, M.D., Dean	55
	56	Ohio State University College of Medicine, Columbus	Pub.	1914	630.00	None	4 Years or Arts—Med.	151	141	136	141	569	140	Charles A. Doan, M.D., Dean	56
Okla.	57	University of Oklahoma School of Medicine, Oklahoma City	Pub.	1900	500.00	1,000.00	3	100	92	87	92	371	93	Mark R. Everett, Ph.D., Dean	57
Ore.	58	University of Oregon Medical School, Portland	Pub.	1887	603.00	906.00	3	80	73	69	73	295	66	D. W. E. Baird, M.D., Dean	58
Pa.	59	Hahnemann Medical College and Hospital of Philadelphia	Pri.	1848	922.00	922.00	3	109	97	94	93	393	93	Charles S. Cameron, M.D., Dean	59
	60	Jefferson Medical College of Philadelphia	Pri.	1825	982.76	982.76	3	175	164	171	167	677	166	William A. Sodeman, M.D., Dean	60
	61	Temple University School of Medicine, Philadelphia	Pri.	1901	950.00	950.00	3	136	129	124	118	507	115	Robert M. Bucher, M.D., Dean	61
	62	University of Pennsylvania School of Medicine, Philadelphia	Pri.	1765	1,100.00	1,100.00	3	126	122	132	126	506	125	John McK. Mitchell, M.D., Dean	62
	63	Woman's Medical College of Pennsylvania, Philadelphia	Pri.	1850	1,075.00	1,075.00	3 (4 Preferred)	51	46	42	41	180	41	Marion Fay, Ph.D., Dean	63
	64	University of Pittsburgh School of Medicine	Pri.	1883	1,096.00	1,096.00	3	101	98	96	83	378	80	Francis S. Cheever, M.D., Dean	64
Puerto Rico	65	University of Puerto Rico School of Medicine, San Juan	Pub.	1949	558.00	558.00	3	55	48	45	45	193	43	Jose R. Vivas, M.D., Dean	65
S.C.	66	Medical College of South Carolina, Charleston	Pub.	1823	592.50	No Nonresident Freshmen	3	80	73	73	73	299	74	John T. Cuttino, M.D., Dean	66
Tenn.	67	University of Tennessee College of Medicine, Memphis	Pub.	1851	567.00	912.00	3	202	189	136	131	658	173	Maston Kennerly Callison, M.D., Dean	67
	68	Meharry Medical College, Nashville	Pri.	1876	791.00	791.00	3	74	59	68	68	269	67	Daniel T. Rolfe, M.D., Dean	68
	69	Vanderbilt University School of Medicine, Nashville	Pri.	1873	1,010.00	1,010.00	Bachelor's Degree or Senior in Absentia	52	51	48	48	199	48	John W. Patterson, M.D., Dean	69
Tex.	70	University of Texas Southwestern Medical School, Dallas	Pub.	1943	360.00	360.00	4	101	98	104	94	397	91	Atticus J. Gill, M.D., Dean	70
	71	University of Texas Medical Branch, Galveston	Pub.	1887	350.00	None	4	143	112	142	132	529	132	Kenneth M. Earle, M.D., Dean	71
	72	Baylor University College of Medicine, Houston	Pri.	1900	997.50	997.50	3	84	84	69	73	310	73	Stanley W. Olson, M.D., Dean	72
Utah	73	University of Utah School of Medicine, Salt Lake City	Pub.	1905	480.00	830.00	3	57	55	46	48	206	48	Philip B. Price, M.D., Dean	73
Vt.	74	University of Vermont College of Medicine, Burlington	Pub.	1822	550.00	1,500.00	4 and a Bachelor's Degree	51	50	44	40	185	40	George A. Wolf, M.D., Dean	74
Va.	75	University of Virginia School of Medicine, Charlottesville	Pub.	1825	514.00	964.00	3	76	71	68	66	281	68	Thomas H. Hunter, M.D., Dean	75
	76	Medical College of Virginia, Richmond	Pub.	1838	671.00	1,021.00	3	85	78	96	95	354	94	William F. Maloney, M.D., Dean	76
Wash.	77	University of Washington School of Medicine, Seattle	Pub.	1945	438.00	768.00	3	75	74	73	69	291	68	George N. Aagaard, M.D., Dean	77
Wis.	78	University of Wisconsin Medical School, Madison	Pub.	1907	380.00	730.00	3	101	93	75	71	340	71	John Z. Bowers, M.D., Dean	78
	79	Marquette University School of Medicine, Milwaukee	Pri.	1913	950.00	950.00	3	105	87	93	95	380	95	John S. Hirschboeck, M.D., Dean	79
		Totals						7,818	7,186	7,071	6,872	28,977	6,860		
		Approved Schools of Basic Medical Sciences													
N.H.	1	Dartmouth Medical School, Hanover	Pri.	1797	1,400.00	1,400.00	3	24	24	...	...	48		Rolf C. S	
N.D.	2	University of North Dakota School of Medicine, Grand Forks	Pub.	1905	206.00	476.00	3	41	34	...	...	75		Theodore	
S.D.	3	State University of South Dakota School of Medicine, Vermillion	Pub.	1907	436.00	736.00	3	44	35	...	...	79		Walter L	
W.Va.	4	West Virginia University School of Medicine, Morgantown	Pub.	1902	316.00	752.00	3	41	33	...	...	74		Edward	
		Totals						150	126	...	...	276			
		Schools Developing New Programs*													
Fla.	1	University of Florida College of Medicine, Gainesville	Pub.	1956	600.00	1,200.00	4	50	47	40	...	137		George T	
N.J.	2	Seton Hall College of Medicine and Dentistry, Jersey City	Pri.	1956	950.00	950.00	3	80	73	71	...	224		Charles J	
		Totals						130	120	111	...	361			
		Grand Totals						8,128	7,432	7,182	6,872	29,614			

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* Provisionally approved on the basis of full implementation of the first two years' program.
1. Nonresidents of other approved medical schools are considered for advanced standing. The nonresident tuition and fees are $755.
2. Covers fees. There is no tuition.
3. Nonresidents of other approved medical schools are considered for advanced standing. Fees are $1592.50.

f approved four-year schools in full operation to 79. Two newly developing schools, Uni- y of Florida College of Medicine and Seton l College of Medicine and Dentistry, had third-year students for the first time in 1958-1959. With classes first graduating in 1959-1960, those two schools will increase the number of fully operational approved four-year medical schools to 81. There remains four two-year schools of basic medical sciences. West Virginia University expects to enroll its third-year class for the first time in the 1960-1961 academic year. The University of Kentucky medical school expects to enroll first year medical students for the first time in 1960.

The 12 approved Canadian medical schools all present a full four-year program.

Construction Completed.—Major projects completed during the year by 25 medical schools in the United States totaled $70,305,429. Construction included 12 new facilities or expansion and/or renovation of old facilities primarily for research, 9 primarily for teaching, 9 clinical facilities, and 4 dormitories. New basic science buildings were completed by Howard, Michigan, and Southwestern. The University of Florida completed construction of its teaching hospital in October, 1958, and the University Hospital at Seattle, started in 1956, was partially completed and occupied in March, 1959, with total completion scheduled for October, 1959.

Construction Initiated.—Twenty-seven medical schools initiated major projects estimated at approximately 54 million dollars for construction and 5 million dollars for equipment. Construction initiated includes 20 new facilities or expansion and/or renovation of old facilities primarily for research, 5 primarily for teaching, 6 clinical facilities, and 2 dormitories. The University of California at Los Angeles has initiated construction of a neuropsychiatric institute to house the clinical, teaching, and research facilities for the Department of Psychiatry and the Divisions of Neurology, Neurosurgery, and Neuropathology. Teaching and research buildings have been initiated by Dartmouth, Bowman Gray, North Dakota, University of Pennsylvania, Woman's, and Washington University.

Construction Planned for 1959-1960.—Major projects planned for initiation in 1959-1960 with funds already committed is estimated at approximately 49 million dollars for construction and 5 million dollars for equipment. Such construction is being planned by 31 schools and includes 21 new facilities or expansion and/or renovation of old facilities primarily for research, 8 primarily

TABLE 2.—*Approved*

Province		Approved Medical Schools	Year Organized	Tuition: Resident	Tuition: Non-resident	Premedical Requirement*
Alta.	1	University of Alberta Faculty of Medicine, Edmonton	1913	393.25 (1st yr.) 503.25 (2nd yr.) 553.25 (3-4-yrs.)	Same	3
B.C.	2	University of British Columbia School of Medicine, Vancouver	1949	545.00	Same	3
Man.	3	University of Manitoba Faculty of Medicine, Winnipeg	1883	531.00	Same	3
N.S.	4	Dalhousie University Faculty of Medicine, Halifax	1867	531.00	731.00	3
Ont.	5	Queen's University Faculty of Medicine, Kingston	1854	430.00 A† 545.00 B	Same	1‡
	6	University of Western Ontario Faculty of Medicine, London	1881	625.00	Same	3
	7	University of Ottawa Faculty of Medicine, Ottawa	1945	559.00	859.00	1‡
	8	University of Toronto Faculty of Medicine, Toronto	1843	591.50 (1-2-3 yrs.) 601.50 (4th yr.)	Same	1‡§
Que.	9	McGill University Faculty of Medicine, Montreal	1828	750.00	Same	3§
	10	University of Montreal Faculty of Medicine, Montreal	1843	545.00	630.00	Degree
	11	Laval University Faculty of Medicine, Quebec	1852	520.00	Same	Degree
Sask.	12	University of Saskatchewan College of Medicine, Saskatoon	1926	475.00 (1st yr.) 525.00 (2-3-4 yrs.)	Same	3
		Totals				

* Number of premedical years required after Junior matriculation in high school for admission to medical school.

† A, premedicine; B, medicine.

‡ In the case of Queen's, Ottawa, and Toronto, where years of premedical college work is under the Faculty of Medicine in addition to the four years of medical school itself, the figure given admits to the first premedical college year of the faculty. To enter the four-year medical school program directly, two years of college are needed in addition to the figure given.

CONSTRUCTION OF FACILITIES

The annual reports from the medical schools indicate that during 1958-1959, 56 institutions in the United States and 5 in Canada initiated, completed, or have funds committed for construction and equipment of new facilities. Table 3 summarizes this information. This study indicates that there has been a significant decrease since last year[9] in estimated costs for projects initiated or planned, although there was a definite increase in the expenditures for completed construction. The number of institutions in the United States engaged in expansion of their facilities was fewer by four as compared with results published last year. The number of institutions in Canada remained the same. In the United States, 27 schools indicated the initiation of 35 construction projects, 25 schools completed construction of 39 projects, and 31 schools have funds committed for construction of 40 projects with construction to begin in 1959-1960.

for teaching, 4 clinical facilities, and 2 student dormitories. University of California at Los Angeles will begin construction of a Nuclear Medicine Building to provide permanent and more adequate quarters for the fundamental and applied medical research programs. The new building will permit programs which have to do with radiation effects and atomic medicine to expand their graduate student complement. Clinical research buildings are in the planning stage at the University of Chicago, University of Kansas, Louisville, Tulane, North Carolina, Oregon, Tennessee, Vanderbilt, and Baylor. A rehabilitation and ambulatory diagnostic patient facility will be constructed by the University of Rochester, while Duke is embarking on the construction of a center for the study of aging. The University of Nebraska has completed plans for a patient service, teaching and research building.

In Canada, Queen's University completed a clinical teaching and research building and Laval completed its basic science building. Alberta has initiated a substantial addition to its medical school building and British Columbia has funds committed for construction of a new medical sciences building.

POTENTIAL SITES FOR NEW MEDICAL SCHOOLS

In a recent session the legislature of the State of Texas authorized the establishment of a new four-year medical school in San Antonio. The new school will be a part of the University of Texas, which is presently engaged in studies directed toward determination of the most appropriate location for the new institution. Although the school will be an integral part of the University, the legislature indicated that the community of San Antonio will be expected to provide the necessary clinical facilities.

There are other groups and institutions that have indicated varying degrees of interest and activity directed toward the development of additional medical schools. The incidence and timing of actual future establishment of new schools cannot be predicted.

The Council on Medical Education and Hospitals in collaboration with the Association of American Medical Colleges makes every effort to be of as much assistance as possible to those groups and institutions which contemplate development of new schools of medicine. Consultative visits to St. Paul, Minnesota, and Albuquerque, New Mexico, will be made in regard to the possible establishment of new educational facilities at those sites.

Medical Schools in Canada

1st Premedical Year	2nd Premedical Year	1st Year	2nd Year	3rd Year	4th Year	Required Intern Year	Total	Graduates 5-1-58 to 6-30-59		
...	...	54	57	52	54	...	217	50	Walter C. MacKenzie, M.D., Dean	1
...	...	57	49	60	47	...	213	44	John F. McCreary M.D., Dean	2
...	...	51	56	55	56	...	218	55	Lennox G. Bell, M.D., Dean	3
...	...	60	58	51	52	50	221¶	52	C. B. Stewart, M.D., Dean	4
52	51	63	53	54	56	...	226¶	56	G. H. Ettinger, M.D., Dean	5
...	...	60	60	54	54	...	228	51	James B. Collip, M.D., Dean	6
18	32	68	63	52	56	...	239¶	55	Jean-Jacques Lussier, M.D., Dean	7
128	118	163	152	139	147	...	601¶	147	J. A. MacFarlane, M.D., Dean	8
...	...	110	103	98	107	...	418	98	Lloyd G. Stevenson, M.D., Dean	9
...	...	142	102	112	102	...	458	97	Wilbrod Bonin, M.D., Dean	10
...	...	124	128	109	141	123	502¶	124	Jean-Baptiste Jobin, M.D., Dean	11
...	...	34	30	31	32	...	127	30	J. Wendell Macleod, M.D., Dean	12
198	201	986	911	867	904	173	3,068¶	859		

§ Degree in arts and sciences if college work is taken elsewhere.
‖ A very definite preference is given to those who have baccalaureate degrees.
¶ Intern and premedical figures not included.

MEDICAL SCHOOL EXPENDITURES

Information regarding the financing of medical school activities is presented again on the same basis as in last year's report. Figures given in table 4 may be compared with those in table 15 in 1958 report on Medical Education in the United States and Canada but they cannot and should not be compared with what appeared to be somewhat similar data in earlier reports because current data have an entirely different base.

Mr. A. J. Carroll, Business Officer, State University of New York Upstate Medical Center is now engaged in a cost accounting study of all medical schools. This study is designed to relate on a uniform basis medical school expenditures to the specific programs supported. The study is being conducted under the auspices of the Association of American Medical Colleges with support from the Kellogg Foundation. When the results of Carroll's study are reported, for the first time there will be available an accurate accounting of medical school expenditures, the costs of the various programs supported and the sources of the funds expended.

It is necessary to emphasize again the defects and limitations of the data presented in table 4. The greatest doubt as to accuracy in reflecting grand totals of actual and estimated expenditures rests in the lack of uniform accounting practices and terminology. For example, there is no generally accepted method of accounting for direct costs of patient care in teaching hospitals. Without question, in certain instances some such costs are included, and in others they are not a part of the individual school expenditures that are reflected in these totals.

When these data were presented a year ago, readers were cautioned that because of varying accounting practices, the data could be broken down to indicate with any validity the percentage of total expended funds that originated in any listed source. Despite this warning, organizations and individuals that should know better did utilize the data to purport to present the per cent of total medical school expenditures which were received from state appropriations, general university funds, tuition and fees and overhead on grants, etc.

Table 3.—*Estimates of Costs for Construction of Facilities in United States and Canada, 1958-1959*

	No. of Schools	Estimated Construction Cost*	Estimated Equipment Cost	Total
United States				
Construction Initiated	27	$53,524,132	$5,186,389	$58,710,521
Construction Completed ...	25	63,044,731	7,260,698	70,305,429
Construction Planned†	31	48,867,545	5,165,805	53,033,350
Canada				
Construction Initiated	3	2,690,735	717,000	3,407,735
Construction Completed ...	3	1,353,772	422,605	1,776,377
Construction Planned	2	2,810,500	153,000	2,963,500

* A few schools reported equipment costs as part of construction costs.

† Funds already committed and construction planned for 1959-1960.

As was pointed out before, all medical schools receive funds from students as payment for tuition and fees, yet 27 schools report no funds expended from this item. In almost all of these 27 institutions, student fees and tuition are reported under such other sources as general university funds, or state appropriation. The same situation prevails particularly for funds reported under the sources of state appropriation, general university funds and overhead on grants. Funds secured from these sources are reported as expended under any one of three or four different sources depending on the individual school's accounting practices. Furthermore any given school's practices may vary from year to year as attested by the differences on the numbers of schools indicating funds expended from specific sources between this report and that of a year ago.

A comparison of total expenditures for 1957-1958 with those of the previous year shows an increase of 17% (approximately 40 million dollars) which is just slightly higher than was anticipated in the estimate made at the time. Expenditures for the academic year 1958-1959 are presently estimated to increase by 11% to a total of 311 million dollars.

The total actual expenditure for the median four year school for 1957-1958 was $2.795 million. This represents an increase in funds expended by the median four year school of approximately $400,000 since last year. The total estimated expenditure for the median four year school for 1958-1959 is $3.220 million.

Table 4.—*Medical School Expenditures (United States)**

Source of Funds	Number of Schools Reporting Item	Actual Expenditures 1957-1958	Number of Schools Reporting Item	Estimated Expenditures 1958-1959
(a) Federal Grants for Research	85	$ 59,313,527.86	85	$ 70,247,770.06
(b) Non-government Gifts and Grants for Research ...	85	33,119,441.75	85	35,794,903.31
Sub-total items (a) and (b)		92,432,969.61		106,042,673.37
(c) Federal Grants for Teaching (include both institutional and individual grants)	83	14,530,648.75	83	18,258,345.12
(d) Non-government gifts and grants for teaching (include both institutional and individual gifts and grants)	68	7,466,034.94	69	8,050,272.60
Sub-total Items (c) and (d)		21,996,683.69		26,308,617.72
(e) Unrestricted gifts and grants	57	6,331,464.45	56	6,689,335.55
(f) State, County or City Appropriation for defrayal of medical school expenses	35	34,535,897.12	36	37,866,674.63
(g) State, County or City subsidies paid to the university or medical school as partial reimbursement for medical college costs	18	4,361,410.50	15	4,324,631.97
(h) General University funds..	55	41,362,854.16	55	44,686,161.68
(i) Endowment Income	51	17,513,786.12	51	18,522,494.61
(j) Tuition and Fees	58	17,708,341.30	57	18,577,029.35
(k) Overhead on Grants	48	5,223,188.56	49	6,310,395.79
(l) Teaching expenses (faculty and supporting staff, salaries, and related supplies and expenses) paid by hospitals, clinics, etc.	36	17,313,485.90	34	17,708,540.04
(m) Teaching expenses paid from medical service funds	16	5,523,164.31	17	6,932,040.15
(n) Actual or estimated costs of services and expenses provided to Medical College by the university without charge (administrative, buildings and grounds, library, student health and other services)	33	10,528,900.16	32	12,295,088.91
(o) Other	27	4,642,874.73	26	4,744,940.95
Sub-total items (e) through (o)		165,048,367.31		178,657,333.63
Total items (a) through (o)	85	279,478,020.61	85	311,008,624.72

* See accompanying text for defects and limitations of these data.

It seems pertinent to re-emphasize that data presented for medical school expenditures in terms of present knowledge cannot be translated into costs of educating medical students—or indeed any other single function of medical schools. These meaningful interpretations will be possible only when there is available a uniform, functional cost accounting system such as is under study by Carroll.

Canadian schools' expenditures are not presented since the returns were not complete for this information.

TEACHING RESPONSIBILITIES OF MEDICAL SCHOOL FACULTIES FOR OTHER THAN MEDICAL STUDENTS

Table 5 portrays by school and category of student the teaching responsibilities of faculties of medicine for students other than medical students in 1958-1959. The total of 85,459 is almost three

Table 5.—*Teaching Responsibilities for*

		Undergraduates or Basic Professional Enrollment						Professional Enrollment		
	Medical Schools in the United States	Dental Students	Pharmacy Students	Nurses	Technical Students	Arts and Science Majors	Other	Interns	Residents	Postgraduate Continuation Students[1]
1	Medical College of Alabama	103	..	155	61	..	31	28	85	21
2	University of Arkansas School of Medicine	..	..	..	35	..	..	38	69	..
3	College of Medical Evangelists	119	..	40	83	..	..	179	279	115
4	University of California School of Medicine, Los Angeles	..	..	183	21	20	82	26	133	3,500
5	University of Southern California School of Medicine, Los Angeles	..	120	..	120	75	..	152	192	3,100
6	Stanford University School of Medicine	..	..	99	75	..	..	44	182	250
7	University of California School of Medicine, San Francisco	289	281	173	50	..	..	45	226	3,000
8	University of Colorado School of Medicine	..	..	200	13	21	..	60	210	3,955
9	Yale University School of Medicine	..	..	19	6	..	..	53	160	126
10	Georgetown University School of Medicine	357	..	102	..	..	37	14	104	
11	George Washington University School of Medicine	..	10	..	9	199	..	25	56	14
12	Howard University College of Medicine	247	132	25	23	3	9	15	45	7
13	University of Miami School of Medicine	..	..	278	24	..	..	64	210	..
14	University of Florida College of Medicine	..	..	..	..	..	83	3	12	2
15	Emory University School of Medicine	83	..	30	24	..	38	63	185	13
16	Medical College of Georgia	..	..	..	2	..	6	4	109	4
17	Chicago Medical School	..	..	..	..	..	..	20	28	..
18	Northwestern University Medical School	..	..	175	32	..	..	19	174	105
19	Stritch School of Medicine of Loyola University	..	..	..	..	..	47	10	34	..
20	University of Chicago, The School of Medicine	..	..	..	..	..	..	36	146	2
21	University of Illinois College of Medicine	250	200	61	22	..	..	63	259	..
22	Indiana University School of Medicine	149	..	304	68	..	..	12	142	910
23	State University of Iowa College of Medicine	137	116	203	90	505	35	20	160	619
24	University of Kansas School of Medicine	1	..	116	32	68	..	21	121	5,623
25	University of Louisville School of Medicine	223	..	252	24	..	86	21	96	5
26	Louisiana State University School of Medicine	..	..	54	21	..	18	51	297	322
27	Tulane University School of Medicine	..	..	285	..	..	..	100	175	422
28	Johns Hopkins University School of Medicine	..	..	250	..	..	..	87	222	134
29	University of Maryland School of Medicine and College of Physicians and Surgeons	..	55	60	..	..	..	32	136	215
30	Boston University School of Medicine	..	..	76	15	131	..	17	121	12
31	Harvard Medical School	30	..	..	..	..	..	70	460[2]	463[2]
32	Tufts University School of Medicine	200	..	..	..	..	..	57	124	30
33	University of Michigan Medical School	95	33	110	75	50	281	51	329	2,441
34	Wayne State University College of Medicine	..	..	..	15	..	..	61	150	262
35	University of Minnesota Medical School	282	24	91	451	356	..	33	211	1,230
36	University of Mississippi School of Medicine	..	..	50	18	..	..	24	32	364
37	University of Missouri School of Medicine	..	..	207	4	81	775	..	27	..
38	Saint Louis University School of Medicine	213	..	225	293	..	..	1	72	5
39	Washington University School of Medicine	..	..	..	..	..	42	61	195	91
40	Creighton University School of Medicine	90	..	115	7	..	..	13	27	..
41	University of Nebraska College of Medicine	..	..	35	19	..	..	11	51	..
42	Dartmouth Medical School	..	..	162	36	7	..	16	65	1
43	Seton Hall College of Medicine and Dentistry	84	..	..	..	..	..	67	96	..
44	Albany Medical College of Union University	2	..	237	4	..	31	43	89	116
45	University of Buffalo School of Medicine	120	125	180	40	8	..	49	130	404
46	Albert Einstein College of Medicine of Yeshiva University	..	..	200	36	..	38	37	208	..
47	Columbia University College of Physicians and Surgeons	150	..	349	86	..	198	24	256	813
48	Cornell University Medical College	..	..	210	..	..	..	72	280	7
49	New York Medical College, Flower and Fifth Avenue Hospitals	..	..	136	..	..	..	113	169	43
50	New York University College of Medicine	160	..	450	..	12	..	55	407	1,620

[1] Approximate annual enrollment at regularly presented short courses, seminars, and lectures. Undoubtedly, a considerable amount of duplication of individuals appears.

[2] Count incomplete. Year did not end until Aug. 31, 1959.

[3] Clinical subjects only.

times the total number of medical students (29,614) and is 32% higher than the figure reported by and estimated for the schools one year ago. The Council has more faith in the validity of the figures for this year for other teaching responsibilities than it has had in previous years. As has been pointed out in the two previous years, schools benefit in terms of budgetary support and understanding by presenting as fully as possible the true extent of their total teaching responsibilities.

It should be noted that, except for dental students, interns, and residents, other students do not require from faculty members the same expenditure of energy and time as do medical students. For

Other than Medical Students, 1958-1959

		Undergraduates or Basic Professional Enrollment						Professional Enrollment		
		Dental Students	Pharmacy Students	Nurses	Technical Students	Arts and Science Majors	Other	Interns	Residents	Postgraduate Continuation Students
51	State University of New York Downstate Medical Center, New York City	..	..	..	..	..	..	129	254	1,200[6]
52	University of Rochester School of Medicine and Dentistry	..	..	230	19	123	100	51	124	9
53	State University of New York Upstate Medical Center, Syracuse	..	..	..	..	..	..	34	121	675
54	University of North Carolina School of Medicine	193	122	200	49	16	120[5]	138	118	595[4]
55	Duke University School of Medicine	..	..	327	46	48	..	61	215	..
56	Bowman Gray School of Medicine of Wake Forest College	..	..	145	36	..	75	15	75	10
57	University of North Dakota School of Medicine	..	..	105	12	44	11	..	..	..
58	University of Cincinnati College of Medicine	..	..	165[3]	..	..	..	52	173	35
59	Western Reserve University School of Medicine	189	..	255	12	..	..	67	290	158
60	Ohio State University College of Medicine	378	51	369	154	217	1,164	24	202	85
61	University of Oklahoma School of Medicine	..	..	95	25	..	..	20	122	1,634
62	University of Oregon Medical School	..	..	276	22	..	13	28	84	388
63	Hahnemann Medical College and Hospital of Philadelphia	..	..	39	23	..	22	18	65	..
64	Jefferson Medical College of Philadelphia	..	..	252	18	23	..	33	100	162
65	Temple University School of Medicine	..	..	285	30	..	..	..	116	12
66	University of Pennsylvania School of Medicine	260	..	30	74	66	49	50	268	250
67	Woman's Medical College of Pennsylvania	..	..	76	..	..	..	12	25	10
68	University of Pittsburgh School of Medicine	9	..	107	..	..	..	12	255	178
69	University of Puerto Rico School of Medicine	55	..	..	19	..	..	24	70	..
70	Medical College of South Carolina	..	100	182	13	..	9	28	57	259
71	State University of South Dakota School of Medicine	..	..	17	1	100	..	3	4	..
72	University of Tennessee College of Medicine	395	195	112	86	..	53	48	97	..
73	Meharry Medical College	107	..	89	29	..	..	12	24	..
74	Vanderbilt University School of Medicine	..	..	..	..	..	..	32	79	..
75	University of Texas Southwestern Medical School	..	..	..	..	..	..	75	231	747[2]
76	University of Texas Medical Branch	..	..	160	42	..	..	39	153	266
77	Baylor University College of Medicine	..	..	60	..	..	57	32	201	20
78	University of Utah School of Medicine	..	31	95	39	52	300	30	69	53
79	University of Vermont College of Medicine	..	..	48	27	..	16	13	40	1
80	University of Virginia School of Medicine	..	..	220	..	..	..	34	103	129
81	Medical College of Virginia	294	213	288	79	..	14	51	121	..
82	University of Washington School of Medicine	300	150	719	326	624	781	42	112	1,119
83	West Virginia University School of Medicine	33	47	..	9	..	5	..	..	..
84	University of Wisconsin Medical School	..	65	182	172	41	24	14	115	775
85	Marquette University School of Medicine	329	..	..	212	..	..	18	159	72
	Totals	5,926	2,100	11,115	3,514	2,890	4,650	3,419	11,998	39,817
	Medical Schools in Canada									
1	University of Alberta Faculty of Medicine	90	100	45	17	200	100	25	49	4
2	University of British Columbia School of Medicine	..	42	160	35	50	34	33	70	39
3	University of Manitoba Faculty of Medicine	20	..	250	..	..	..	45	23	23
4	Dalhousie University Faculty of Medicine	26	21	29	..	..	13	52	54	3,393
5	Queen's University Faculty of Medicine	..	..	24	13	6	..	32	14	7
6	University of Ottawa Faculty of Medicine	..	..	17	..	..	..	26	17	4
7	University of Western Ontario Faculty of Medicine	..	..	127	..	..	..	..	..	..
8	University of Toronto Faculty of Medicine	167	165	34	383	49	..	121	..	155
9	McGill University Faculty of Medicine	150	..	100	..	275	120	75	311	190
10	University of Montreal Faculty of Medicine	90	107	..	108	..	94	102	..	26
11	Laval University Faculty of Medicine	..	..	325	39	..	..	141	69	12
12	University of Saskatchewan College of Medicine	..	87	132	33	4	41	12	46	1
	Totals	543	525	1,263	628	584	402	664	653	3,854

4. Duplicating figure of approximately 100 between these categories.
5. 76 graduate students (nonmedical), 44 in School of Public Health.
6. 583 are physicians attending short postgraduate courses given at school and out in the state.

instance, 100 registrants in a postgraduate course for physicians may require only relatively little time by a few faculty members in a year. A class of 100 student nurses may involve only a few of the medical faculty for a small number of lecture hours a year. This may be similarly the case with pharmacy students, arts and science majors, and technical students. On the other hand, a class of dental students may involve the basic medical science faculty to the same extent in time and energy as does a class of medical students. Interns and particularly residents exact a large expenditure of time and energy by the faculty members who are in those clinical services of the major teaching hospital(s).

Just as true cost accounting is helpful in presenting a meaningful picture of expenditures that can be of material assistance in securing understanding and support of budgetary needs, so would a similar approach in the apportionment of effort among the various teaching responsibilities be of assistance to the medical schools and to those who need to understand them. It is hoped that in the next year, a way will be developed for securing this kind of information, possibly in relation to the 1960-1961 year.

It should also be pointed out that, except for interns and residents, the numbers given for students other than medical students probably are larger than the number of people involved because of duplication. This is known to be true in postgraduate courses, in which the numbers represent enrollments and not the actual number of physician-registrants in nearly all cases. It is likely to be true with arts and science students, in which one student may register in more than one course in which the medical faculty participates, as well as with technical students. A student nurse in a degree program may be counted once as a nurse and again as an arts and sciences student. It is likely, therefore, that the total of 85,459 does not represent that number of individuals for whom medical faculties have had some teaching responsibilities in 1958-1959. This reservation as to the import of the numbers should be borne in mind in relation to the text that follows.

Of the total of 85,459 reported as other than medical students, 13% are students in nursing, 18% interns and residents and 47% are physicians in continuation education courses.

The 11,145 students in nursing involved the faculties of 65 medical schools. Sixty-four schools reported physicians in postgraduate courses, 61 schools reported 3,514 technical students, 34 schools reported 5,926 dental students and 4,650 "other" students, the faculties of 25 schools had 2,890 arts and sciences students, and 19 schools had pharmacy students for which the medical faculties had some teaching responsibility. All of the four-year medical schools except two (Temple and Missouri) reported interns, and the faculty personnel of all of the four year schools had teaching responsibilities for residents.

Six of the 81 four-year medical schools reported no students in the categories of dental, pharmacy, technical, nursing, arts and sciences majors, and other.

Counting all schools, including even those reporting only one physician in postgraduate courses, 64 schools were active in this field in 1958-1959, with a total of 39,817 enrollments. For all 64 schools, the average enrollment was 622 and the median was 160. The following tabulation presents this kind of information more adequately.

Number of Enrollments by Physicians	*Number of Schools*
1 - 20	17
21 - 100	8
101 - 500	21
501 - 1,000	7
1001 - 2,000	5
over - 2,000	6
	64

For the 47 medical schools having more than 20 enrollments of physicians in postgraduate courses in 1958-1959, the average enrollment for the year was 844 and the median was 294.

Table 5 also portrays the medical faculty teaching responsibilities for other than medical students for the Canadian schools. The schools reporting on this item had a total of 9,116 students, although the same reservations regarding duplication of individuals are probably as applicable to the Canadian schools as to those in the United States. This would also be the case in regard to the faculty time and energy requirement by other than medical students, with again the exception of dental students, interns and residents.

Students in nursing, physicians in continuation courses, and interns and residents accounted for 71% of all the students in addition to medical students, as compared to 78% in schools in the United States. The major difference was in the proportion of interns and residents reported in the two countries, with Canadian schools reporting 4% fewer in this category. Pharmacy students comprised a larger proportion of the additional students burdening medical faculties in Canadian schools, composing 5.7% of the total as compared to 2.5% in the United States. Technical students also loomed larger relatively in the teaching responsibilities of Canadian medical faculties, comprising 7% of additional students, which is almost twice the proportion they occupied in the United States.

Only one of the Canadian schools had no teaching responsibilities for other than medical students and nursing students. Six of the schools reported dental students, six schools reported pharmacy students, 11 schools reported student nurses, 7 of the

12 schools reported technical students, six reported arts and sciences majors, six reported students not otherwise categorized, 11 had interns among the teaching responsibilities of their medical faculties, and nine had residents. It is interesting that 11 schools reported physicians in continuation education courses with only five of the schools each having fewer than 20 enrollments.

GRADUATE EDUCATION IN THE BASIC MEDICAL SCIENCES

In addition to data secured in the previous three years regarding enrollments and degrees granted in the basic medical sciences, this year information was obtained from medical schools in the United States and Canada about the number of positions that were available in advanced degree programs. Table 6 presents the data by school, field, and program for the 1958-1959 year. The increasing number of unfilled budgeted faculty positions in the current 85 medical schools in the United States and 12 in Canada, as well as the prospect of additional schools lends greater importance to medicine each year of programs that provide the advanced education required for the production of additional teachers and investigators qualified to fill academic posts.

It is encouraging that the total enrollments in doctorate degree programs were 12% greater in 1958-1959 than in 1957-1958 in medical schools in the United States, and that enrollments in postdoctorate programs had increased 64% (table 6). Enrollments in masters degree programs were about the same as in preceding years. However, the total number of degrees granted in the various fields was fractionally lower, with 5% fewer masters degrees and 8.5% fewer doctorate degrees (Ph.D., Sc.D.) being awarded in 1958-1959 than in the previous year.

When the total positions available in graduate programs in the basic medical sciences were compared with total enrollments, it became evident that programs are generally available for additional students if they can be attracted into such preparation. There were about 30% more total positions available in masters and doctorate programs than there were students enrolled in 1958-1959, while there were 74% more postdoctorate positions available than were enrolled. There were greater surpluses of positions available as compared to students enrolled in doctorate programs in anatomy, biophysics, microbiology, and physiology than in other fields, the positions being in excess of students by 57%, 66%, 35% and 48%, respectively. There were more than three times as many postdoctorate positions in anatomy than there were students, while biophysics and microbiology postdoctorate programs each could have accommodated more than twice as many fellows as were present.

As table 6 demonstrates, the increased enrollments in masters degree programs in three fields (microbiology, pathology, and physiology) were almost offset by decreased enrollments for the masters degree in the other four fields so that little over-all change occurred in the total masters degree candidates. In doctorate programs, there were increased numbers of students in all of the basic medical sciences excepting biophysics (down 33%) and physiology (down 10%). The postdoctorate programs, on which data is probably incomplete had generally increased enrollments in 1958-1959 except for biophysics, which had fewer than one-half of the postdoctorate enrollments reported in 1957-1958. Where increases occurred, they were usually substantial. The ranges of proportiona amount of increase was 12% to 125% for doctorate programs and 46% to 200% for postdoctorate programs.

The one field in which the number of degrees granted was materially fewer in 1958-1959 than in the previous year was microbiology, in which there were awarded almost one-third fewer masters degrees and about one-fourth fewer doctorate degrees

The 12 Canadian medical schools also showed increases in enrollments in advanced degree educational programs in the basic medical sciences. Tota enrollments in programs leading to a masters degree were 46% greater in 1958-1959 than in 1957-1958 Doctorate program enrollments had an increased total enrollment by 10%. The number of postdoctorate fellows reported by Canadian medica schools in either year was too small to analyze.

In masters degree programs in the Canadian schools in 1958-1959, there were increased enrollments in anatomy, pharmacology, and physiology with decreased enrollments as compared to the previous year in microbiology. The numbers were too small to justify proportional comparison. In doctorate programs, there were increased enrollments in biochemistry and pharmacology, with a decreased enrollment in pathology. As in the case of the United States schools, though there were increased enrollments in advanced degree programs in Canadian medical schools, there were generally a trifle fewer masters and doctorate degrees granted in the basic medical sciences.

The Canadian schools had more positions available for graduate study than there were students enrolled. The positions available in masters degree programs were 21% greater than the enrollments while the positions available in doctorate programs were 12% greater than the number of students enrolled.

GRADUATE DEGREE PROGRAMS IN THE CLINICAL FIELDS

Table 7 presents the information reported for the 1958-1959 year by medical schools in the United States and Canada regarding masters degree and doctorate degree (other than M.D.) programs, enrollments, and degrees granted in clinical fields of work. A total of 34 medical schools in the United States (5 more than in 1956-1957) and 7 in Canada reported having masters and/or doctorate degree programs.

There were 32 schools in the United States in 1958-1959 with masters degree programs in clinical areas having a total enrollment of 1,240, while 13 schools reported having 168 enrolled in doctorate programs. Medicine and its subspecialties, preventive medicine and public health, surgery and surgical specialties accounted for more than four-fifths of enrollments. Not all of the educational programs leading to a masters degree or a doctorate in public health and preventive medicine are included in Table 7 because in a number of instances such programs are unrelated to the medical school, as at the University of Michigan and Harvard, for example.

A total of 22 schools in the United States granted 296 masters degrees, of which 149 or about one-half were in preventive medicine and public health. More than one-half of the 296 degrees were granted by 3 schools (Yale, Tulane, and Minnesota). Masters degrees were awarded in all of the major clinical fields except the combination of psychiatry and neurology.

Of the 24 doctorate degrees granted by 8 schools, 20 were granted by the University of Minnesota. Almost half of the 24 doctorate degrees were in surgery and surgical specialties. Other fields in which doctorates were granted were medicine, medical specialties, neurology, obstetrics and gynecology, and preventive medicine and public health.

Seven of the 12 Canadian medical schools reported having masters degree programs in clinical fields, with a total enrollment of 49, and 14 masters degrees granted in 1958-1959. One Canadian school, McGill, reported doctorate degree programs in clinical fields (experimental medicine and neurology), with an enrollment of 11 and the granting of 5 doctorate degrees in 1958-1959. Of the total of 19 masters and doctorate degrees in clinical fields granted, 18 were awarded by one school, McGill University.

Postgraduate Medical Education

Table 5 and the section entitled "Teaching Responsibilities of Medical School Faculties for Other Than Medical Students" presents information about the schools and physician enrollments in postgraduate continuation education programs in 1958-1959. No special study was conducted in the past year relative to enrollments and courses by all organizations and institutions active in that field because of the special study reported only two years ago and earlier in 1959.[10]

In 1958-1959 the 64 medical schools in the United States having programs of continuation education reported a total of 39,817 enrollments. The much larger size of this figure in relation to reports in previous years indicates that this may represent more complete data although it may also represent the larger role of medical schools in continuation education of physicians.

MEDICAL SCHOOL FACULTIES

Questions were included in the annual questionnaire to medical schools this year about numbers and status of total full-time faculty personnel regarding degrees held, academic rank, and numbers by department and rank of full-time faculty who received 50% or more of their salaried income from federal research and/or training grants exclusive of residents and fellows. The information published annually since 1949 regarding vacant faculty positions was also secured this year. In the following text and tables, the information received is presented, analyzed, and discussed.

FULL-TIME FACULTY DEGREES AND NUMBERS

Table 8 presents the status of 10,350 full-time faculty personnel by department and degree in the 85 medical schools in the United States. Pathology department faculty members are not included in either basic medical science or clinical department subtotals in this and succeeding tables unless otherwise stated because pathology departments have attributes of each group rather than predominantly of one or the other.

For the past 20 years at least there are no previous data on faculty degrees for all medical schools with which the 1958-1959 information can be compared.

For the total of 10,350 full-time faculty, 6,546 (or 63%) had the M.D. degree, 2,788 (or 27%) had the Ph.D. degree, and 466 (or 4.5%) had both degrees. As would be expected, the majority of M.D.'s (5,935 or 91%) were in clinical departments and pathology. If those with both the M.D. and Ph.D. are counted with the M.D. group, the proportion of M.D.'s remains the same, 91%, in the clinical departments and pathology.

A possibly unexpected finding was that 605 faculty members with the Ph.D. are in clinical departments, comprising 9% of clinical faculty personnel. If those with a Ph.D. in addition to the M.D. degree are included, then 12.6% of full-time clinical faculty people have the Ph.D. degree. This figure is identical with the proportion of Ph.D. faculty personnel in clinical departments reported in the NIH Study of Twenty Medical Schools. Approximately half of these are in the 2 departments of preventive medicine and psychiatry.

Although more than two-thirds (68%) of full-time faculty personnel in the basic medical science departments hold only the Ph.D. degree, another 7% have both degrees. Thus, from one point of view, three-fourths of full-time personnel in these depart-

TABLE 6.—*Advanced Degree and Postdoctoral Prog*

POSITIONS AVAILABLE

	Masters									Doctorates									Postdoctorates							
United States	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other
Medical College of Alabama	1	2	..	1	1	..	1	..	6	3	6	..	..	..	1	2	..	12	..	..	..	..	..	..	..	..
University	..	5	..	1	2	..	2	..	10	..	1	..	..	..	1	..	..	2	..	..	..	..	..	..	..	..
College of	4	5	..	4	..	3	5	..	21	4	5	..	..	..	2	5	..	16	..	..	..	..	..	..	..	..
University	2	..	2	..	..	10	3	..	17	15	15	10	..	..	8	5	..	53	..	..	..	..	..	..	3	..
University of Southern California	5	16	..	9	1	3	12	..	46	5	18	..	3	..	5	10	..	41	5	2	..	6	..	2	2	..
Stanford University	..	..	..	5	..	..	2	..	7	1	..	..	9	..	1	4	..	15	..	..	..	..	..	..	1	..
University of California, San Francisco	5	..	..	..	..	..	4	..	9	10	19	..	1	..	..	12	..	42	3	..	..	..	..	..	4	..
University of Colorado	..	..	..	..	..	3	..	..	3	6	4	10	10	..	6	7	..	43	1	3	5	..	..	3	1	..
Yale University	..	..	..	2	..	..	..	..	2	15	20	..	15	..	15	15	..	80	4	4	..	3	..	8	4	..
Georgetown University	4	4	..	4	2	2	..	..	16	..	2	..	3	2	9	2	..	18	..	..	..	..	..	..	..	..
George Washington University	3	17	..	13	..	4	..	..	37	4	19	..	20	..	10	6	..	59	..	..	..	..	..	..	3	..
Howard University	..	..	..	..	..	6	1	..	7	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Miami	8	8	..	8	..	6	6	..	36	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Florida	4	5	..	..	..	..	6	..	15	2	5	..	..	..	..	4	..	11	2	3	..	1	..	..	3	..
Emory University	15	12	..	12	..	12	12	..	63	15	12	..	12	..	12	12	..	63	4	2	..	2	..	4	4	..
Medical College of Georgia	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Chicago Medical School	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Northwestern University	9	9	..	2	6	4	8	..	38	4	9	..	6	3	4	7	..	33	4	8	..	3	20	1	..	..
Stritch School of Medicine	5	..	..	6	..	..	6	..	17	7	16	..	2	..	8	3	..	36	..	..	..	..	..	..	1	..
University of Chicago	7	7	..	15	6	1	5	..	41	8	13	9	20	6	13	6	..	75	1	12	..	2	..	4	1	..
University of Illinois	10	11	..	9	3	11	12	..	56	3	15	..	3	..	8	7	..	36	..	..	..	..	..	..	..	..
Indiana University	..	..	..	..	..	..	..	..	..	..	..	..	12	..	..	..	..	12	..	..	..	..	..	..	..	..
State University of Iowa	5	6	..	..	..	6	5	..	22	3	8	..	12	..	3	12	..	38	2	3	..	..	..	..	3	..
University of Kansas	4	2	..	8	..	..	7	..	21	9	8	..	7	..	5	2	..	31	..	2	..	2	..	1	..	..
University of Louisville	1	10	..	6	1	5	2	..	25	..	10	..	2	..	3	6	..	21	..	5	..	1	7	3	2	..
Louisiana State University	3	4	..	2	..	..	4	..	13	3	4	..	2	..	..	4	..	13	1	1	..	1	..	..	3	..
Tulane University	2	7	..	5	..	6	14	2	36	1	6	..	6	..	3	1	..	17	..	..	..	..	..	..	..	..
Johns Hopkins University	..	..	..	..	..	..	..	..	..	1	3	..	..	..	..	3	..	7	..	..	..	..	..	..	..	..
University of Maryland	..	..	..	1	..	1	..	..	2	5	10	..	3	..	3	3	..	24	..	..	..	..	..	..	..	..
Boston University	2	..	..	2	..	1	3	..	8	2	10	..	3	..	5	3	..	23	1	2	..	1	1	1	..	..
Harvard Medical School	..	..	..	..	..	..	..	..	..	1	18	1	14	1	4	3	..	42	..	18	..	..	..	..	..	..
Tufts University School of Medicine	..	..	..	..	..	..	..	..	..	..	10	..	..	..	4	7	..	21	..	3	..	..	..	2	2	..
University of Michigan	8	10	..	16	..	4	4	4	46	8	25	..	22	..	22	5	6	88	..	10	..	2	..	4	5	4
Wayne State University	..	10	..	5	10	..	..	8	33	2	10	..	2	..	..	..	8	22	..	4	..	..	..	..	..	4
University of Minnesota	5	6	..	11	..	2	23	11	61	11	28	..	23	..	10	14	6	92	..	..	..	..	..	..	..	..
University of Mississippi	..	4	..	8	..	2	10	..	24	..	4	..	2	..	2	2	..	10	..	..	..	..	..	..	..	..
University of Missouri	2	7	..	10	..	..	5	..	24	2	7	..	2	..	..	5	..	16	..	..	..	..	..	..	2	..
Saint Louis University	3	3	..	..	..	..	..	..	6	..	17	..	3	..	2	2	..	24	..	..	..	..	..	..	..	..
Washington University	..	..	..	..	2	..	..	..	2	5	2	..	4	2	7	3	..	23	..	2	..	1	12	10	1	..
Creighton University	6	..	..	8	..	..	..	..	11	..	2	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..
University of Nebraska	3	2	..	..	..	..	..	..	5	2	1	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..
Dartmouth Medical School	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Seton Hall College of Medicine & Dentistry	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Albany Medical College of Union University	..	1	..	..	..	..	1	..	2	..	6	..	3	..	3	3	..	15	..	..	..	..	..	..	..	..
University of Buffalo	4	3	..	4	..	5	5	..	21	3	3	..	6	..	4	6	..	22	4	2	..	6	..	1	6	..
Albert Einstein College of Medicine	..	..	..	..	..	..	..	..	..	5	6	..	..	..	8	..	..	19	5	6	..	3	1	6	..	..
Columbia University	..	..	..	..	..	..	..	..	..	12	30	..	10	..	2	10	..	64	..	..	..	..	..	..	..	..
Cornell University	3	3	..	3	..	3	3	10	25	3	3	..	3	..	3	3	20	35	4	5	..	3	..	4	4	10
New York Medical College	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
New York University	1	4	..	..	..	..	..	..	5	1	9	..	3	4	..	..	..	17	..	..	..	..	..	..	..	..
State University of New York, New York City	1	..	..	..	..	1	1	..	3	2	3	..	..	..	5	5	..	15	..	..	..	..	..	..	..	..
University of Rochester	3	9	33	8	2	3	4	..	62	2	9	25	8	2	3	12	..	61	5	3	10	3	3	2	2	..
State University of New York, Syracuse	..	..	..	3	..	..	2	..	5	6	2	..	4	..	3	3	..	18	..	1	..	2	..	1	2	..
University of North Carolina	..	4	..	10	2	..	1	..	17	..	10	..	8	2	..	4	..	24	..	7	..	6	2	..	..	..
Duke University	10	..	..	2	..	..	..	..	12	3	30	..	4	..	..	..	..	37	2	8	..	2	..	..	..	..
Bowman Gray School of Medicine	1	1	..	2	..	..	2	..	6	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of North Dakota	6	6	..	4	..	..	..	5	21	4	4	..	..	..	..	..	1	9	..	..	..	..	..	..	..	..
University of Cincinnati	..	..	..	..	1	..	2	..	3	5	1	..	1	..	5	3	..	15	..	..	..	..	..	..	2	..
Western Reserve University	1	..	..	..	..	..	1	..	2	5	6	..	12	3	5	10	..	41	2	6	..	4	7	..	4	..
Ohio State University	15	..	..	..	14	..	15	10	54	8	..	..	..	6	..	10	10	34	..	..	..	..	..	..	..	..
University of Oklahoma	2	2	..	3	1	1	2	..	11	1	5	..	4	..	2	..	..	12	..	..	..	..	..	..	..	..
University of Oregon	7	13	..	2	..	12	10	..	44	..	5	..	..	..	..	..	..	5	..	..	..	..	..	..	..	..
Hahnemann Medical College	5	9	..	8	5	4	2	..	33	2	7	..	3	2	3	3	..	20	1	5	..	4	1	1	3	..
Jefferson Medical College	10	..	..	2	..	5	6	..	23	6	2	..	6	..	6	6	..	26	4	2	..	2	..	2	2	..
Temple University	..	..	..	1	..	..	1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Pennsylvania	..	..	..	12	..	1	3	..	16	2	7	6	29	..	1	18	..	63	..	2	22	1	..	..	..	..
Woman's Medical College	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..
University of Pittsburgh	..	15	..	..	..	..	..	6	21	10	10	..	7	..	..	..	6	33	..	3	..	2	..	..	..	2
University of Puerto Rico	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Medical College of South Carolina	1	..	..	..	..	4	..	..	5	3	1	..	..	..	2	2	..	8	..	..	..	..	..	..	..	..
State University of South Dakota	2	2	..	5	..	..	..	2	11	1	1	..	1	..	..	..	..	3	..	..	..	1	..	..	..	..
University of Tennessee	1	11	..	2	6	3	5	..	28	4	2	..	1	1	4	13	..	25	..	..	..	..	..	..	..	..
Meharry Medical College	..	2	..	2	2	..	2	..	8	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Vanderbilt University	1	5	..	..	..	1	..	..	7	6	10	..	4	..	10	10	..	40	2	5	..	3	..	3	10	..
University of Texas Southwestern Medical School	2	3	..	8	..	..	..	..	13	6	3	..	3	..	..	..	..	12	1	1	..	1	..	..	..	..
University of Texas Medical Branch	3	2	..	3	..	1	2	..	11	3	1	..	4	..	1	4	..	13	..	..	..	..	..	..	..	..
Baylor University	12	10	..	10	..	3	10	..	45	6	10	..	10	..	3	2	..	31	..	..	..	..	..	..	..	..
University of Utah	3	..	..	12	..	..	..	..	15	6	20	..	10	..	5	2	..	43	..	..	..	3	..	4	4	..
University of Vermont	1	..	..	2	..	..	2	..	5	..	3	..	..	..	4	..	..	7	..	..	..	..	..	2	..	..
University of Virginia	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Medical College of Virginia	1	2	..	1	..	..	2	1	7	3	2	2	..	2	2	1	..	12	..	..	..	..	..	..	..	..
University of Washington	1	2	..	10	..	2	..	..	15	..	28	..	10	..	5	17	..	60	..	6	..	..	..	5	18	..
West Virginia School of Medicine	6	5	..	7	..	5	5	..	28	..	2	..	3	..	2	2	..	9	4	2	..	3	..	2	2	..
University of Wisconsin	3	8	..	8	21	10	8	..	58	3	7	..	7	20	10	7	..	54	..	7	..	..	13	..	7	..
Marquette University	3	6	..	8	12	..	12	..	41	3	2	..	3	2	4	6	..	20	2	4	..	..	2	4	4	..
Totals	236	300	35	318	100	156	271	59	1,475	282	612	63	390	58	281	344	57	2,087	64	159	37	77	69	83	115	20
Canada																										
University of Alberta	1	3	..	1	..	..	2	..	7	..	1	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..
University of British Columbia	1	2	..	..	..	2	5	..	10	..	1	..	..	..	2	..	..	3	..	..	..	..	..	..	..	..
University of Manitoba	1	4	..	2	2	5	2	..	16	..	2	..	2	..	5	..	..	9	..	2	..	2	..	3	..	..
Dalhousie University	..	7	..	4	..	4	5	..	20	..	3	..	..	..	2	2	..	7	..	..	..	..	..	..	..	..
Queen's University	1	2	..	1	3	1	4	..	12	..	1	..	1	..	..	1	..	3	..	..	..	..	..	..	..	..
University of Ottawa	1	1	..	2	..	..	..	..	4	1	1	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..
University of Western Ontario	1	4	..	..	..	2	2	2	11	..	3	3	1	..	..	1	1	9	..	..	..	..	..	..	..	..
University of Toronto	2	8	..	..	..	5	6	..	21	2	11	..	..	..	5	8	..	26	..	..	..	..	..	..	..	..
McGill University	7	7	..	3	..	1	6	7	31	3	31	..	6	1	4	6	3	54	..	..	..	..	..	..	..	..
University of Montreal	1	3	..	2	..	..	4	5	15	..	1	..	2	..	..	1	3	7	..	..	..	..	..	..	..	..
Laval University	..	3	..	..	..	..	1	..	4	..	8	..	..	..	..	..	..	8	..	..	..	..	..	..	..	1
University of Saskatchewan	2	3	..	1	4	..	..	2	12	1	3	..	..	1	..	..	2	7	..	..	..	..	..	..	..	..
Totals	18	47	..	16	9	20	37	16	163	7	66	3	12	2	18	19	9	136	..	3	..	2	..	3	..	1

and Enrollments in the Basic Medical Sciences

PROGRAMS and ENROLLMENT																											DEGREES AWARDED, 1958-1959																	
Masters									Doctorates									Postdoctorates									Masters									Doctorates								
Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total	Anatomy	Biochemistry	Biophysics	Microbiology	Pathology	Pharmacology	Physiology	Other	Total
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151	235	33	250	73	101	240	41	1,124	180	512	38	289	51	229	233	55	1,590	19	97	18	35	69	50	64	7	359	41	48	23	58	15	24	50	8	267	29	78	8	52	9	32	43	7	258
1	3	..	1	..	..	2	..	7	..	1	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..	1	1	2	..	..	..	..	..	..	3	..	1	..	..	..	..	..	..	1
1	2	..	..	..	2	5	..	10	..	1	..	..	..	2	..	..	3	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	1	..	3	..	..	..	..	..	..	..	..	..
1	1	..	2	2	4	2	..	12	..	1	..	..	..	2	..	..	3	..	..	..	2	..	2	..	..	4	..	2	..	..	..	..	..	..	2	..	..	..	..	..	1	..	..	1
..	1	..	..	..	..	..	..	1	..	2	..	1	..	1	..	..	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	1
1	2	..	1	3	1	4	..	12	..	1	..	1	..	..	1	..	3	..	..	..	..	..	..	..	..	..	..	2	..	1	2	1	1	..	7	..	..	..	..	..	..	2	..	2
1	1	..	2	..	..	..	..	4	1	1	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1	4	..	..	..	2	2	2	11	..	3	3	1	..	..	1	1	9	..	..	..	..	..	..	..	..	..	1	2	..	..	..	..	..	..	3	..	3	1	..	..	..	..	..	4
2	8	..	..	..	5	6	..	21	..	11	..	..	..	5	8	..	24	..	..	..	..	..	..	..	..	..	..	4	..	..	..	2	3	..	9	2	5	..	..	..	..	2	..	9
7	7	..	3	..	1	6	7	31	3	31	..	6	1	4	6	3	54	..	..	..	..	..	..	..	..	..	..	..	..	1	..	1	1	..	3	..	7	..	3	..	..	3	1	14
1	3	..	2	..	..	4	5	15	..	1	..	2	..	..	1	3	7	..	..	..	..	..	..	..	..	..	..	1	..	2	..	..	..	..	3	..	..	..	1	..	..	..	..	1
..	3	..	..	..	..	1	..	4	..	8	..	..	..	..	..	..	8	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
1	1	..	..	2	..	..	1	5	1	1	..	..	..	..	..	1	3	..	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	2	..	..	..	..	..	..	..	..	..
17	36	..	11	7	15	32	15	133	5	62	3	11	1	14	17	8	121	..	1	..	2	..	2	..	..	5	2	16	..	4	3	4	6	..	35	2	16	1	5	..	1	7	1	[illegible]

ments have the Ph.D. degree. On the other hand it might be said that more than one-fourth (27%) of the full-time basic medical science faculty earned the M.D. degree. Table 8 presents subtotals for the basic medical science departments before and after including pathology in order to stress the skewing effect that the preponderance of M.D.'s in pathology would have. The NIH Study of Twenty Medical Schools included pathology as a preclinical department, giving 34.9% M.D.'s and 60.3% Ph.D.'s in the preclinical departments.

It is obvious that in the basic medical science departments of medical schools, the 2,335 faculty personnel having the Ph.D. degree comprise a large and important group. Their importance in the basi medical sciences has increased concomitant wit the great expansion of significant and highly complex knowledge in these fields, a body of knowledg and research techniques requiring full-time stud to master to the point of advancing into new frontiers. The increasing inter-action of the basic medical science and clinical fields in the research study and understanding of disease processes probably is the most important factor accounting for the "pure" Ph.D. personnel in the clinical departments. Biochemistry, genetics, microbiology, pharmacology, and physiology—all with the aid of biophysics and biostatistics—are making increasingly important

TABLE 7.—*Advanced Degree Program*

	*Programs Available																	
	Masters									Doctorates								
	Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties	Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties
UNITED STATES																		
College of Medical Evangelists	✓	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..
University of California, Los Angeles	✓	..	..	..	✓	..	✓	✓	..	..	..	..	..	..	..	✓	..	..
University of Colorado	✓✓	..	✓	..	✓	..	..	✓	✓	..	..	..	..	..	..	..	..	..
Yale University	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	✓	..	..
University of Chicago	..	..	✓	✓	..	..	..	✓	✓	..	..	..	..	..	..	..	..	✓
University of Illinois	✓	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	✓
State University of Iowa	..	..	..	..	..	..	✓	..	✓✓✓✓	..	..	..	..	..	..	✓	..	..
Tulane University	✓	..	✓	✓	✓	..	✓	✓	✓✓✓	..	..	..	..	..	..	✓	..	..
Tufts University School of Medicine	✓	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	✓
University of Michigan	✓	✓	..	..	✓	..	..	..	✓✓	..	..	..	..	..	..	..	..	..
University of Minnesota	✓✓✓	✓	✓	✓	✓	..	✓	✓	✓✓✓✓✓	✓✓✓	✓	✓	✓	✓	..	✓	✓	✓✓✓ ✓✓✓
University of Mississippi	✓	..	..	..	..	..	✓	..	✓	..	..	..	..	..	..	..	..	..
Creighton University	✓	..	✓	✓	..	✓	..	✓	✓	..	..	..	..	..	..	..	..	..
Columbia University	..	..	..	..	..	..	✓	..	..	✓	..	..	..	..	..	✓	..	..
Cornell University	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	✓	..	..
New York Medical College	✓	..	✓	✓	..	..	..	✓	✓✓✓✓	..	..	..	..	..	..	..	..	..
New York University	✓	..	..	..	..	..	..	..	✓✓✓✓✓	..	..	..	..	..	..	..	..	✓
State University of New York, New York City	..	..	..	..	✓	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Rochester	✓	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Cincinnati	✓	..	..	✓	..	..	✓	..	✓	..	..	..	..	..	..	✓	..	..
Western Reserve University	..	..	..	✓	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Ohio State University	✓	..	✓	..	✓	..	✓	✓	✓✓	..	..	..	..	..	..	..	..	..
University of Oklahoma	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Temple University	✓	✓	✓	..	..	..	..	..	✓✓✓✓	..	..	..	..	..	..	..	..	..
University of Pennsylvania	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Puerto Rico	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..	..	..
University of Tennessee	..	..	✓	✓	..	..	..	..	✓✓✓	..	..	..	..	..	..	..	..	..
University of Texas Southwestern Medical School	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..	..
University of Texas Medical Branch	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	✓	..	..
Baylor University	✓	..	..	..	✓	..	..	..	..	..	..	..	..	..	..	..	..	..
University of Virginia	..	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..
University of Washington	..	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..
University of Wisconsin	✓	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Marquette University	✓✓	..	✓	..	..	..	..	✓	✓✓	..	..	..	..	..	..	..	..	..
Totals	*19	*3	*10	*8	*8	*1	*12	*10	*20	*2	*1	*1	*1	*1	*0	*9	*1	*5
CANADA																		
University of Alberta	..	..	✓	✓	✓	..	..	..	✓	..	..	..	..	..	..	..	..	..
University of Manitoba	✓	..	..	✓	✓	..	..	..	✓	..	..	..	..	..	..	..	..	..
University of Western Ontario	✓	..	✓	✓	✓	..	✓	..	✓	..	..	..	..	..	..	..	..	..
University of Toronto	..	..	..	..	✓	..	..	..	..	..	..	..	..	..	..	..	..	..
McGill University	✓	✓	..	..	..	..	..	..	✓	✓	✓	..	..	..	..	..	..	..
University of Montreal	..	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..
Laval University	..	..	..	..	..	..	..	..	✓	..	..	..	..	..	..	..	..	..
Totals	3	1	2	3	4	0	1	0	6	1	1	0	0	0	0	0	0	0

* Programs rather than position available are presented in this portion of the table; while the vertical totals represent the number of schools that reported degree programs in each field. Multiple checks in medicine and in surgery columns represent programs in sub-specialties in these fields.

contributions to advancing knowledge at the gross, cellular, subcellular, and molecular levels of the organism.

An analysis (table 9) was prepared of the distribution of degrees held by full professors and department chairmen as compared to the full-time basic medical science faculty as a whole, excluding pathology. Whereas 407 or 50% of the 814 department heads and full professors had the M.D. degree, whether or not they also held the Ph.D. degree, about 27% of the total full-time basic medical science faculty had the M.D. degree. With the large reservoir of Ph.D. faculty (2,111) who have come into the basic medical science departments of medical schools, it is likely that an increasing proportion of the senior faculty in the future will be Ph.D. rather than M.D. personnel.

Table 10 presents for 11 of the 12 Canadian medical schools information about numbers of full time faculty by degree and department. For the reason previously outlined for United States schools, pathology is listed after rather than with the basic medical science departments.

For the 586 full-time faculty as a whole in all departments, 358 or 61% had the M.D. degree, 138 or almost 24% had the Ph.D. degree, and 63 or 11% had both degrees.

and Enrollment in the Clinical Sciences

Programs and Enrollments																				Degrees Awarded																			
Masters										Doctorates										Masters										Doctorates									
Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties	Total	Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties	Total	Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties	Total	Medicine & Medical Specialties	Neurology	Obstetrics and Gynecology	Pediatrics	Psychiatry	Psychiatry and Neurology	Preventive Medicine & Public Health	Radiology	Surgery and Surgical Specialties	Total
2	..	..	..	..	..	..	..	4	6	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	2	2	..	..	..	..	..	..	..	..	..	0
4	..	..	..	3	..	1	2	..	10	4	..	..	..	..	..	1	..	..	5	1	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	0
21	..	8	..	2	..	..	3	9	43	..	..	..	..	..	..	..	..	..	0	6	..	1	..	..	..	..	1	..	8	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	48	..	..	48	..	..	..	..	..	..	3	..	..	3	..	..	..	..	..	..	40	..	..	40	..	..	..	..	..	..	3	..	..	3
..	..	..	..	..	..	..	..	2	2	..	..	..	..	..	..	..	..	3	3	..	..	..	..	..	..	..	..	2	2	..	..	..	..	..	..	..	..	1	1
1	..	..	..	..	..	..	..	1	2	..	..	..	..	..	..	..	..	..	0	1	..	..	..	..	..	..	..	1	2	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	3	..	36	39	..	..	..	..	..	..	4	..	..	4	..	..	..	..	..	..	1	..	3	4	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	57	..	..	57	..	..	..	..	..	..	15	..	..	15	..	..	..	..	..	..	51	..	..	51	..	..	..	..	..	..	..	..	..	0
1	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
2	6	..	..	3	..	..	..	14	25	..	..	..	..	..	..	..	..	..	0	2	3	..	..	3	..	..	..	7	15	..	..	..	..	..	..	..	..	..	0
256	22	23	21	31	..	4	51	343	751	24	6	1	5	2	..	1	3	55	97	29	2	1	..	..	..	1	2	27	62	2	2	1	..	..	..	..	..	5	10
2	..	..	..	..	..	..	..	2	4	..	..	..	..	..	..	..	..	..	0	2	..	..	..	..	..	..	..	2	4	..	..	..	..	..	..	..	..	..	0
8	..	5	1	..	..	..	2	9	25	..	..	..	..	..	..	..	..	..	0	..	..	2	..	..	..	..	1	..	3	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	47	..	..	47	2	..	..	..	..	..	5	..	..	7	..	..	..	..	..	..	42	..	..	42	2	..	..	..	..	..	2	..	..	4
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
2	..	..	..	..	..	..	..	48	50	..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	5	5	..	..	..	..	..	..	..	..	1	1
..	..	..	..	..	..	..	..	..	0	..	..	..	..	3	..	..	..	..	3	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
3	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	0	3	..	..	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	7	..	..	7	1	..	..	..	..	..	18	..	4	23	..	..	..	..	..	..	3	..	..	3	..	..	..	..	..	..	1	..	2	3
..	..	..	2	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	0	..	..	..	2	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	0
12	..	12	..	28	..	10	1	36	99	..	..	..	..	..	..	..	..	..	0	3	..	3	..	2	..	1	1	9	19	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	3	..	..	3	..	..	..	..	..	..	3	..	..	3	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	1	..	..	1
..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	0	5	..	1	..	..	..	..	..	6	12	..	..	..	..	..	..	..	..	1	1
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	10	..	..	10	..	..	..	..	..	..	..	..	..	0
..	..	2	1	..	..	..	..	6	9	..	..	..	..	..	..	..	..	..	0	..	..	..	1	..	..	..	..	2	3	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	2	..	2	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	3	..	..	..	..	3	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	2	2	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	2	2	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
314	29	50	25	70	0	180	59	513	1,240	31	6	1	5	5	0	52	5	63	168	52	6	8	3	5	0	149	5	68	296	4	2	1	0	0	0	7	0	10	24
..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
4	..	..	1	4	..	..	..	1	10	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	1	..	..	..	1	..	..	2	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
15	6	..	..	1	..	..	..	8	30	9	2	..	..	..	..	..	..	..	11	6	2	..	..	..	..	..	..	5	13	3	2	..	..	..	..	..	..	..	5
..	..	..	..	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
..	..	..	..	..	..	..	..	5	5	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0	..	..	..	..	..	..	..	..	..	0
19	6	1	1	5	0	1	0	16	49	9	2	0	0	0	0	0	0	0	11	6	2	0	0	0	0	1	0	5	14	3	2	0	0	0	0	0	0	0	5

As in the case of United States medical schools, about one-eighth of the full-time clinical faculty had the Ph.D. degree. However, in Canadian schools a larger proportion of basic medical science faculty personnel had the M.D. degree (52.5%) than in United States schools (27%).

TABLE 8.—*Full-Time Faculty Personnel by Fields and Degrees Held in Medical Schools in the United States*

Field	M.D.		Ph.D.		Both		Other		Total	
	No.	%	No.	%	No.	%	No.	%	No.	%
Anatomy	155	22.0	475	67.3	44	6.2	32	4.5	706	100.0
Biochemistry	46	6.7	582	85.0	35	5.1	22	3.2	685	100.0
Biophysics	12	12.9	66	71.0	3	3.2	12	12.9	93	100.0
Biostatistics	1	...	2	...	1	...	0	...	4	...
Genetics	3	...	4	...	1	...	0	...	8	...
Microbiology	113	20.5	374	67.8	28	5.0	37	6.7	552	100.0
Pharmacology	138	31.8	230	53.0	51	11.7	15	3.5	434	100.0
Physiology	135	23.8	351	61.9	58	10.2	23	4.1	567	100.0
Physiology-pharmacology	8	...	27	...	3	...	1	...	39	...
Subtotal	611	19.8	2,111	68.4	224	7.2	142	4.6	3,088	100.0
Pathology	626	82.6	72	9.5	27	3 6	33	4.3	758	100.0
Subtotal	1,237	32.2	2,183	56.8	250	6.5	175	4.5	3,845	100.0
Medicine	1,497	89 6	80	4 8	57	3.4	37	...	1,671	...
Obstetrics-gynecology	294	90.5	18	5.5	10	3.1	3	...	325	...
Pediatrics	618	88.3	27	3.8	24	3.4	31	...	700	...
Psychiatry	520	64.0	207	25.5	11	1.4	74	...	812	...
Pub. Health-Prev. Med.	192	49.6	85	22.0	19	4 9	91	23.5	387	100.0
Radiology	370	82.8	36	8.1	10	2.2	31	6.9	417	100 0
Surgery	790	90.5	29	3.3	43	4.9	11	1.3	873	100.0
Other clinical	1,028	79.8	123	9.5	41	3.2	97	7.5	1,289	100.0
Subtotal, all clinical	5,309	81 6	605	9.3	215	3.3	375	5.8	6,504	100.0
Over-all totals	6,546	63.3	2,788	26.9	466	4.5	550	5.3	10,350	100.0

The difference in degrees of faculty personnel between Canadian and United States medical schools was marked in pathology departments, also. In the 11 Canadian schools which supplied data, about one-half the full-time pathology faculty personnel had the M.D. degree and about one-half had the Ph.D. degree, while one-eighth had both degrees. For United States schools, 83% of the full-time pathology faculty personnel held the M.D. degree and 13% held the Ph.D. Thus, in the matter of degrees held, Canadian pathology departments resembled more their basic medical science departments, and United States pathology departments resembled more their clinical departments.

In Canadian schools, 76 (or 55%) of the 137 people having Ph.D. degrees but not the M.D. degree were in departments of biochemistry and physiology. These departments in United States schools had only 33% of the "pure" Ph.D. personnel.

In both countries, more than one-fourth of all full-time clinical faculty were in the departments of medicine. In Canada (table 11) the clinical department having the second largest number and proportion of full-time faculty was psychiatry (48 people or 21.5% of all clinical faculty). In the United States, surgery departments were in second place among clinical departments in the use of full-time faculty personnel, having 873 or 13.4% of all full-time clinical faculty.

FEDERAL GRANT SUPPORT OF FULL-TIME FACULTY PERSONNEL

In the special study of medical school faculties this year, a question was included relative to the number of full-time faculty members by academic rank and department who receive 50% or more of their salaried income from Federal research and/or training grants, excluding anyone in resident or fellowship status regardless of faculty title. Table 12 presents the information supplied by the 85 medical schools in the United States, while table 13 provides the information for the 11 Canadian schools which reported data.

A total of 1,392 of the 10,350 full-time faculty, or 13%, in United States medical schools received 50% or more of their salaried income from Federal grants. There was relatively little difference between basic medical science and clinical departments, being 13.3% for the former and 14% for the latter. Pathology had a smaller proportion of its full-time faculty members, only 9.5%, supported to this degree by Federal grants.

TABLE 9.—*Full-Time Faculty by Numbers and Proportions in Departments in Medical Schools in the United States*

Department	Number Persons	% of Total in Basic Sciences	% of Total in Clinical Fields	% Over-all, Total
Anatomy	706	22.9		
Biochemistry	685	22.2		
Biophysics	93	3.0		
Biostatistics	4	*		
Genetics	8	*		
Microbiology	552	17.9		
Pharmacology	434	14.1		
Physiology	567 }1,040	18.4 }33.7		
Pharmacology-physiology	39	1.2		
Total basic sciences	3,088			29.8
Pathology	758	19.7	10.4	7.3
Anesthesiology	302		4.6	
Medicine	1,671		25.7	
Obstetrics-gynecology	325		5.0	
Pediatrics	700		10.8	
Psychiatry	812		12.5	
Public health-preventive med.	387		5.9	
Radiology	447		6.9	
Surgery	873		13.4	
Other clinical†	987		15.2	
Total clinical	6,504		100.0	62.8
Over-all total	10,350			100.0

* Less than 1%.

† Includes dermatology, neurology, ophthalmology, orthopedic surgery, otolaryngology, physical medicine, urology, clinical science, industrial medicine, and rehabilitation.

Biophysics had by far the highest proportion of full-time faculty in this category, 59 or 63% of the faculties in biophysics having 50% or more of their salaries supplied by Federal grants. The next largest categories, having 20.8% so supported, were neurology and/or psychiatry if these be grouped together. Such a grouping was necessary as in the case of physiology-pharmacology in which some schools have combined departments. For psychiatry alone, among schools having a separate department of psychiatry, 30% of the full-time faculty personnel were in this category relative to federal grant support. Physical medicine was in third place, having 25% of its full-time faculty receiving 50% or more of salaried income from Federal grants. Biochemistry had in the basic medical sciences the largest proportion of departmental faculty in this category (16%), about the same as in departments of medicine.

TABLE 10.—*Full-Time Faculty Personnel by Fields and Degrees Held in Medical Schools in Canada*

	M.D.		Ph.D.		Both		Other		Total	
Field	No.	%	No.	%	No.	%	No.	%	No.	%
Anatomy	48	63.1	13	17.1	11	14.5	4	5.3	76	100.0
Biochemistry	7	10.3	50	73.5	7	10.3	4	5.9	68	100.0
Biophysics	1	10.0	7	70.0	1	10.0	1	10.0	10	...
Medical research	1	...	0	...	5	...	0	...	6	...
Microbiology	25	56.8	14	31.8	2	...	3	...	44	...
Pharmacology	12	40.0	12	40.0	5	...	1	...	30	...
Physiology	23	38.3	26	43.3	9	15.0	2	...	60	...
Pharmacology-physiology	0	...	5	...	0	...	0	...	5	...
Subtotal, Basic sciences	117	39.1	127	42.5	40	13.4	15	5.0	299	100.0
Pathology	56	87.5	1	...	5	7.8	2	...	64	...
Subtotal	173	47.6	128	35.3	45	12.4	17	4.7	363	100.0
Medicine	52		5		6		2		65	
Obstetrics-gynecology	14		0		0		1		15	
Pediatrics	24		1		1		1		27	
Psychiatry	37		1		5		5		48	
Surgery	24		0		4		0		28	
Other clinical	34		3		2		1		40	
Subtotal, clinical	185	83.0	10	4.5	18	8.0	10	4.5	223	100.0
Over-all total	358	61.1	138	23.5	63	10.8	27	4.6	586	100.0

It is apparent that, with more than one in every eight full-time faculty members receiving 50% or more of salaried income from federal grants, these grants are important sources of support for medical education and research.

The pattern was somewhat different in 11 Canadian medical schools, where a total of only 17 full-time faculty members, or 3% of the total full-time faculty personnel receive 50% or more of their salaried income from Federal research and/or training grants. Only one of these was in a clinical department, 14 were in basic medical science departments, and 2 in pathology departments (table 13). Nearly one-half of such faculty in Canada were in biochemistry departments.

FULL-TIME FACULTY POSITIONS UNFILLED, 1958-1959

In table 14 is presented information supplied by medical schools in the United States about budgeted but vacant full-time faculty positions in 1958-1959. Almost two-thirds (62%) of the total of 655 vacant positions were in clinical departments. The full-time faculty total vacant positions represented 6% of the 11,005 budgeted full-time faculty positions, both filled and unfilled. There was an increase again in 1958-1959 of total unfilled full-time faculty positions, as there has been each year for the past five years. Table 15 portrays comparative total data for the years 1954-1955 to and including 1958-1959.

In both basic science and clinical departments, approximately one-third of the faculty vacancies were newly budgeted positions, as was the case in the 1957-1958 year. More than two-thirds (68%) of all newly budgeted faculty positions in the basic medical sciences, excluding pathology, were in departments of anatomy, microbiology and pharmacology.

As compared to the 1957-1958 data, there were a total of 10 more vacant positions in the basic medical sciences, with anatomy (up 10), pharmacology (up 3), and pathology (up 2) showing the increases while the other departments had relatively fewer budgeted unfilled positions. The clinical departments had a greater increase in budgeted vacant faculty positions as compared with 1957-1958.

The increase each year in medical school unfilled full-time faculty positions should cause concern. As was pointed out a year ago, the vacancies existing in faculty posts reflect the numbers of faculty personnel required to maintain medical education at its present qualitative level and to produce the present number of graduates. It is certain that expansion of educational programs in medicine to meet the physician needs of an enlarging population will require additional full-time faculty.

TABLE 11.—*Full-Time Faculty by Numbers and Proportions in Departments in Medical Schools in Canada*

Department	Number Persons	% Total in Basic Sciences	% Total in Clinical Fields	% Over-all, Total
Anatomy	76	25.4		
Biochemistry	68	22.7		
Biophysics	10	3.3		
Medical research	6	2.0		
Microbiology	44	14.7		
[illegible]	30	10.0		
[illegible]	60 }95	20.1 }31.8		
[illegible]	5	1.7		
Total basic sciences	299			51.0
Pathology	64			10.9
Medicine	65		29.1	
Neurology	10		4.5	
Obstetrics-gynecology	15		6.7	
Pediatrics	27		12.1	
Psychiatry	48		21.5	
Public health-prev. medicine	13		5.8	
Surgery	28		12.5	
Other clinical*	17		7.6	
Total clinical	223			38.1
Over-all total	586			100.0

* Includes anesthesiology, dermatology, ophthalmology, orthopedic surgery, otolaryngology, physical medicine, radiology, urology

The information from table 6 about advanced-degree programs in the basic medical sciences provides little reason for complacency when the figures are compared with the previous year. Although the number of students in doctorate (Ph.D. or Sc.D.) programs was 12% higher than in 1957-1958, the number of degrees awarded was 8% less. It is encouraging that the number of positions in advanced degree programs was in such a surplus that many more able students could have been accommodated. Of the three basic medical sciences accounting for many of the newly budgeted faculty vacancies, pharmacology showed a significant increase (32%) in students in doctorate programs, and anatomy a more modest increase of 13% in the number of graduate candidates for a doctorate.

TABLE 12.—*Number of Full-Time Faculty in United States by Department and Rank who Receive 50% or More of Their Salaried Income from Federal Research and/or Training Grants**

Department	Professor	Associate Professor	Assistant Professor	Instructor	Total	% Full-Time Faculty
Anatomy	3	9	11	17	40	5.6
Anatomy and microbiology	1	0	0	0	1	...
Biochemistry	3	14	48	46	111	16.2
Biophysics	9	18	17	15	59	63.4
Genetics	0	0	1	0	1	...
Microbiology	0	5	18	35	58	10.5
Microbiology and pathology	1	1	0	0	2	...
Neurological science	0	0	0	1	1	...
Pharmacology	5	9	26	25	65	13.4
Physiology	5	15	26	28	74	
Subtotal, basic medical sciences	27	71	147	167	412	13.3
Pathology	4	16	27	25	72	9.5
Subtotal	31	87	174	192	484	12.6
Anesthesiology	0	0	0	2	2	...
Dermatology	1	2	3	3	9	10.7
Industrial medicine	0	2	0	1	3	23.1
Internal medicine	7	40	117	119	283	20.3
Neurology	1	1	25	18	45	20.8
Neurology and psychiatry	0	1	2	6	9	
Obstetrics and gynecology	0	3	8	12	23	7.1
Ophthalmology	0	4	10	11	25	18.5
Orthopedics	0	0	0	2	2	...
Otolaryngology	0	0	3	6	9	...
Pediatrics	2	9	25	38	74	10.6
Physical medicine	1	3	5	27	36	24.8
Psychiatry	11	38	84	113	246	30.3
Public health and preventive medicine	4	3	21	20	48	12.4
Radiology	3	5	11	5	24	5.4
Rehabilitation	0	0	1	0	1	...
Surgery	2	15	21	27	65	7.4
Urology	0	1	1	2	4	...
Subtotal, clinical	32	127	337	412	908	14.0
Over-all totals	63	214	511	604	1,392	13.4

* Excluding anyone in resident or fellowship status, regardless of faculty title.

Table 16 presents for 11 Canadian medical schools, which supplied the data, information regarding unfilled full-time budgeted faculty positions. The total of 23 vacant posts is 3.8% of the total 609 filled and unfilled full-time faculty places. As in the case of United States schools, only one-third of the vacancies are in newly budgeted positions, although these represent a higher proportion of the clinical faculty vacancies than those in the basic medical sciences. There does not appear to be any departmental concentration of vacant posts either in the clinical fields or in the basic medical sciences.

TOTAL NUMBERS AND OFFICE LOCATION OF ALL M.D. FACULTY

In order to better understand the meaning of the terms "full-time" and "part-time" and their significance in terms of the number of faculty personnel in medical schools in the United States, a part of the special faculty study included a question to all medical schools about the total number of M.D. faculty personnel by rank, location of office, and source of income. The total figures secured are presented in table 17. In each box determined by the intersections of rank and description of office location and income source are three numerals. The first represents the number of faculty so categorized in all basic medical science departments, including pathology, the second represents the number so categorized in all clinical departments, while the last number is the total of the first two. It should be emphasized that this section deals with all M.D. faculty, whether they are considered as full-time, part time or volunteer. The immediately preceding sections on faculty degrees, federal grant support, and vacant faculty posts were limited to full-time faculty personnel.

The total of M.D. faculty personnel in 1958-1959 was 31,190, of which 2,455 were in basic medical science departments and pathology, while 28,735 were in clinical departments. Thus, 92% of the total M.D. faculty held their major appointments in clinical departments. From 67% to 70% of the total M.D. faculty was volunteer unsalaried professional personnel.

TABLE 13.—*Number of Full-Time Faculty in Canada by Department and Rank who Receive 50% or More of Their Salaried Income from Federal Research and/or Training Grants**

Department	Professor	Associate Professor	Assistant Professor	Instructor	Total	% Full-Time Faculty
Anatomy	0	1	0	0	1	...
Biochemistry	0	2	4	1	7	41.2
Medical Research	1	2	0	0	3	...
Microbiology	0	1	1	0	2	...
Physiology	0	0	0	1	1	...
Subtotal, basic medical sciences	1	6	5	2	14	4.7
Pathology	0	1	1	0	2	...
Subtotal	1	7	6	2	16	4.4
Medicine	0	0	1	0	1	...
Subtotal, clinical	0	0	1	0	1	...
Over-all totals	1	7	7	2	17	2.9

* Excluding anyone in resident or fellowship status regardless of faculty title.

At the other extreme, 3,540 or 11% were what is ordinarily called "absolute" full-time, with their only office in the university medical center and income only from the medical school and/or its teaching hospital. About two-thirds (63%) of these were in clinical departments, and one-third in basic medical science departments including pathology. More than half (55%) of the "absolute" full-time M.D. faculty were in the more junior academic positions of instructor and assistant professor.

TABLE 14.—*Budgeted Unfilled Full-Time Faculty Positions in Medical Schools in the United States, 1958-1959*

	Newly Budgeted Positions, No.					Old Positions, No.					Old and New Positions, Total				
Basic Science Departments	Instructor	Assistant Professor	Associate Professor	Professor	Total	Instructor	Assistant Professor	Associate Professor	Professor	Total	Instructor	Assistant Professor	Associate Professor	Professor	Total
Anatomy	9	6	1	1	17	11	11	5	11	38	12	17	6	12	55
Biochemistry .	3	4	0	0	7	4	2	5	2	13	7	6	5	2	20
Biophysics ...	1	0	0	0	1	2	0	4	2	8	3	0	4	2	9
Microbiology .	5	3	2	3	13	10	11	4	2	27	15	14	6	5	40
Pathology ...	3	6	6	1	16	8	18	10	8	44	11	24	16	9	60
Pharmacology	2	7	2	2	13	11	9	2	0	22	13	16	4	2	35
Physiology ...	3	4	3	1	11	7	4	5	2	18	10	8	8	3	29
Other basic science dept.															
Genetics	0	0	1	0	1	0	0	0	0	0	0	0	1	0	1
Subtotals	26	30	15	8	79	53	55	35	27	170	79	85	50	35	249
Clinical Departments															
Anesthesiology	5	1	2	1	9	5	12	2	2	21	10	13	4	3	30
Dermatology .	1	2	0	0	3	0	0	0	0	0	1	2	0	0	3
Medicine	6	9	5	1	21	6	11	7	3	27	12	20	12	4	48
Neurology	3	3	0	0	6	3	3	0	0	6	6	6	0	0	12
Obstetrics-gynecology .	11	4	3	2	20	7	13	2	5	27	18	17	5	7	47
Ophthalmology	0	0	1	1	2	2	3	2	2	9	2	3	3	3	11
Orthopedics ..	0	0	0	0	0	0	1	3	0	4	0	1	3	0	4
Otolaryngology	1	1	0	2	4	2	1	0	0	3	3	2	0	2	7
Pediatrics	3	9	5	3	20	2	7	10	4	23	5	16	15	7	43
Physical medicine	0	0	2	1	3	1	2	0	0	3	1	2	2	1	6
Psychiatry ...	8	8	4	4	24	11	15	8	3	37	19	23	12	7	61
Public Health-Preventive Medicine	3	2	3	2	10	4	9	6	5	24	7	11	9	7	34
Radiology	5	5	1	1	12	8	8	7	1	24	13	13	8	2	36
Surgery	5	7	3	2	17	8	10	10	3	31	13	17	13	5	48
Urology	1	1	0	1	3	4	2	3	0	9	5	3	3	1	12
Other clinical departments	1	0	0	0	1	0	3	0	0	3	1	3	0	0	4
Totals	53	52	29	21	155	63	100	60	28	251	116	152	89	49	406
Subtotals	79	82	44	29	234	116	155	95	55	421	195	237	139	84	655

What would ordinarily be known as "geographical full-time" faculty personnel were the physicians in categories (*b*) or (*b*) and (*c*). If (*d*) also were included, then such faculty personnel would number 3,348 physicians. This represented about one-tenth of the total M.D. faculty. Those in category (*c*), whose only office was in the university medical center and whose income was from salary and unrestricted private practice totalled only 1.7% of all M.D. faculty personnel and only 8% of the total full-time faculty in its broadest interpretation.

Ordinarily, categories (*d*) and (*e*) would be considered part-time faculty members and these totalled 3,027, of which 197 were in basic medical science departments, including pathology. Thus, the part-time faculty composed about 10% of all M.D. faculty or about one-third of all faculty excepting the volunteer unsalaried faculty members.

TABLE 15.—*Budgeted Unfilled Full-Time Faculty Positions in Medical Schools in the United States (1954-1955 to 1958-1959)*

	1954-1955	1955-1956	1956-1957	1957-1958	1958-1959
Anatomy	25	18	22	45	55
Biochemistry	9	8	17	28	20
Biophysics	..	..	..	..	9
Microbiology	14	15	18	41	40
Pathology	27	33	46	58	60
Pharmacology	16	19	17	32	35
Physiology	16	15	21	35	29
Genetics	..	..	..	..	1
Subtotals	107	108	141	239	249
Anesthesiology	5	10	6	24	30
Dermatology	..	..	..	..	3
Medicine	23	28	29	55	48
Neurology	..	..	..	..	12
Obstetrics & Gynecology	14	16	13	28	47
Ophthalmology	..	..	..	..	11
Orthopedics	..	..	..	..	4
Otolaryngology	..	..	..	..	7
Pediatrics	15	12	21	35	43
Physical Medicine	..	..	..	..	6
Psychiatry	30	21	29	55	61
Public health & preventive medicine ..	17	14	19	41	34
Radiology	11	8	..	30	36
Surgery	19	22	42	44	48
Urology	.	..	..	..	12
Other clinical departments	17	12	31	65	4
Subtotals	151	143	190	380	406
Totals	258	251	331	619	655

TABLE 16.—*Budgeted Unfilled Full-Time Faculty Positions in Medical Schools in Canada, 1958-1959*

	Newly Budgeted Positions, No.					Old Positions, No.					Old and New Positions, Total				
Basic Science Departments	Instructor	Assistant Professor	Associate Professor	Professor	Total	Instructor	Assistant Professor	Associate Professor	Professor	Total	Instructor	Assistant Professor	Associate Professor	Professor	Total
Anatomy	1	0	0	0	1	0	1	0	0	1	1	1	0	0	2
Biochemistry	0	0	0	0	0	0	1	0	0	1	0	1	0	0	1
Microbiology	0	1	1	0	2	0	0	0	0	0	0	1	1	0	2
Pathology ..	0	1	0	0	1	0	2	0	1	3	0	3	0	1	4
Pharmacology	0	0	0	0	0	1	1	0	1	3	1	1	0	1	3
Physiology ..	0	0	0	0	0	1	0	1	0	2	1	0	1	0	2
Subtotals ...	1	2	1	0	4	2	5	1	2	10	3	7	2	2	14
Clinical Departments															
Medicine	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1
Obstetrics-gynecology	0	1	0	0	1	0	0	0	0	0	0	1	0	0	1
Pediatrics ...	0	0	0	0	0	1	0	0	0	1	1	0	0	0	1
Physical Medicine ...	0	0	0	0	0	0	1	0	0	1	0	1	0	0	1
Psychiatry ...	0	1	0	0	1	0	1	1	0	2	0	2	1	0	3
Public health—preventive medicine ...	0	0	1	0	1	0	0	0	1	1	0	0	1	1	2
Subtotals ...	0	3	1	0	4	1	2	1	1	5	1	5	2	1	9
Totals	1	5	2	0	8	3	7	2	3	15	4	12	4	3	23

Table 18 presents comparative data in total M.D. faculty numbers in the clinical departments fo 1953-1954 and 1958-1959. There has been surpris ingly little change in all categories and in totals. The greatest change has been an increase in what is ordinarily known as geographical full-time (categories *b* + *c*, clinical), which was up 22% in 1958-1959. Although these faculty members constitute a relatively small proportion of total faculty, they are important in the education and research programs of the schools, which could not readily find budgets for that number of "absolute" full-time faculty.

TABLE 17.—*Faculty Office Location and Source of Income for ALL M.D. Faculty in Basic Medical Science and Clinical Departments in Medical Schools in the United States*

Description	M.D.'s Only					
	Department Head	Professor, not Dept. Head	Associate Professor	Assistant Professor	Instructor*	Subtotals and Totals
(a) Only office in the university medical center, income only from medical school and/or teaching hospital	235† 241‡ 476	191 229 420	287 378 665	339 662 1,001	251 727 978	1,303 2,237 3,540
(b) Only office in the university medical center, income from salary and officially restricted private practice	42 292 334	39 246 285	56 470 526	45 606 651	27 410 437	209 2,024 2,233
(c) Only office in the university medical center, income from salary and unrestricted private practice	2 64 66	6 94 100	4 130 134	1 133 134	3 101 104	16 522 538
(d) Only office in the university medical center, entire income from private practice	0 25 25	1 34 35	2 86 88	0 150 150	2 277 279	5 572 577
(e) Outside private office (with or without medical center office) income from medical school salary and private practice outside medical center	2 115 117	17 217 234	35 337 372	63 758 821	75 831 906	192 2,258 2,450
(f) Outside private office (with or without medical center office) entire income from private practice outside medical center	2 144 146	35 1,160 1,195	94 2,363 2,457	196 5,704 5,900	239 11,016 11,255	566 20,387 20,953
(g) Other	5 7 12	18 70 88	22 151 173	67 188 255	52 319 371	164 735 899
Totals of Faculty in all categories Basic Science Departments						2,455
Clinical Departments						28,735
Over-all						31,190

* Excluding anyone in resident or fellowship status, regardless of faculty title.
† In each instance, the first number represents the total in basic medical science departments.
‡ The second number in each case is the total number of persons in the category in the clinical departments.

In regard to the arrangements between schools and faculty members having private practice privileges (categories *b*, *c*, and *d*), the schools were queried as to whether all, some, or none of the faculty members in each category paid the schools for use of the office and services. Table 19 presents the responses of 69 schools in the United States. The lines do not add horizontally to total 69 because some schools reported a certain number of faculty as paying "all," and other faculty members as paying "some" or "none," having interpreted these to mean proportion paid rather than proportion of faculty paying. Dual interpretation blurs somewhat the significance of the responses when combined, although trends are apparent. The 69 schools also did not complete all parts, thus accounting for totals less than 69.

TABLE 18.—*Comparison of Clinical Faculty Numbers*

Status*	United States		Canada	
	1953-1954†	1958-1959‡	1953-1954§	1958-1959‖
(1) Absolute full-time	2,153	2,237	25	76
(2) Geographical full-time	2,078	2,546	32	135
(3) Part-time	2,876	2,830	498	790
(4) Volunteer	21,328	21,122	620	367
	28,435	28,735	1,175	1,368

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* Using categories that are generally meaningful and which were used in 1953-1954 report (J.A.M.A. 156:147 [Sept. 11] 1954). For 1958-1959 year, (1) from category **a**, table 17, (2) from **b** + **c**, (3) from **d** + **e**, (4) or volunteer fom **f** + **g**
† 74 four-year schools and 6 two-year schools.
‡ 81 four-year schools and 4 two-year schools.
§ 11 four-year schools and 1 two-year school.
‖ 12 four-year schools.

A total M.D. faculty numbering 31,190 was reported for 1958-1959. A total of 185,317 M.D.'s in practice were listed in the current American Medical Directory. Consequently, about one in six (17%) of the practicing medical profession have some kind of faculty appointment in one or more of the 85 medical schools in the United States. This represents a significant segment of the medical profession who had a demonstrated and active interest in basic medical education and research.

TABLE 19.—*Number of Schools* in the United States in Which the Faculty Members Pay the Medical School for Use of the Office and Services in the Case of:*

In table 17, category as follows	Senior Faculty*†	Junior Faculty†
(b)	All, 10; some, 6; none, 64	All, 10; some, 5; none, 65
(c)	All, 5; some, 7; none, 46	All, 3; some, 8; none, 46
(d)	All, 3; some, 4; none, 40	All, 3; some, 2; none, 39

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* Total number of schools responding to this was 69.
† Senior faculty—prof. and assoc. prof.; Junior faculty—asst. prof. and instructor.

Table 20 portrays for 11 of the 12 approved Canadian medical schools similar information about total M.D. faculty. There was a total of 1,584 physicians, with 1,368 or 86% of them in the clinical fields. A slightly larger proportion of total M.D. faculty held appointments in basic medical science departments of Canadian schools than was the case in the United States schools.

The prevailing pattern for the basic medical science departments, including pathology, appeared in Canada to be absolute full-time (category *a*), accounting for more than three-fourths (77%) of M.D. faculty in those departments. The predominant category in the clinical fields was (*e*), in which the faculty member had his office and private practice outside the medical center, although he received some salary from the school or hospital. This accounted for 58% of the clinical M.D. faculty reported; with the addition of category (*f*), which constituted unsalaried volunteer faculty members, the proportion was increased to 82% of the total M.D. faculty personnel, similar to the 79% that categories (*e*) and (*f*) amount to of M.D. faculty in United States schools.

Table 20.—*Faculty Office Location and Source of Income for ALL M.D. Faculty in Basic Medical Science and Clinical Departments in 11 Medical Schools in Canada*

	M.D.'s Only					
Description	Department Head	Professor, not Dept. Head	Associate Professor	Assistant Professor	Instructor*	Subtotals and Totals
(a) Only office in the university medical center, income only from medical school and/or teaching hospital	50† 11‡ 61	10 2 12	33 12 45	42 16 58	31 32 63	166 76 242
(b) Only office in the university medical center, income from salary and officially restricted private practice	0 27 27	0 3 3	0 23 23	0 21 21	0 10 10	0 87 87
(c) Only office in the university medical center, income from salary and unrestricted private practice	1 7 8	1 0 1	0 4 4	0 31 31	0 3 3	2 48 50
(d) Only office in the university medical center, entire income from private practice	0 0 0	0 0 0	0 1 1	0 0 0	0 0 0	0 1 1
(e) Outside private office (with or without medical center office) income from medical school salary and private practice outside medical center	0 27 27	1 24 25	6 123 129	12 225 237	11 390 401	30 789 819
(f) Outside private office (with or without medical center office) entire income from private practice outside medical center	0 0 0	0 0 0	0 0 0	0 2 2	0 327 327	0 329 0 329
(g) Other	1 1 2	1 0 1	1 5 6	9 13 22	6 19 25	18 38 56
Totals of faculty in all categories:						
Basic medical science departments						216
Clinical departments						1,368
Over-all						1,584

* Exclude anyone in resident or fellowship status, regardless of faculty title.
† Number of faculty members in category in basic medical science departments.
‡ Number of faculty members in category in clinical departments.

It seems evident from the data reported for United States and Canadian schools regarding faculty personnel that the full time pattern of staffing is present to a greater extent, particularly in clinical departments in United States schools as compared to the Canadian medical schools. However, table 18 comparing clinical faculty numbers in 1958-1959 with numbers from a 1953-1954 study reveals the threefold to fourfold increase in full-time M.D. faculty in clinical departments in Canadian schools in the past five years. Concomitant with the increase in absolute and geographical full-time clinical faculty as well as a 59% increase in part-time salaried faculty, there has been a decrease in numbers in the volunteer unsalaried faculty category, a decrease of 41%. The total clinical faculty personnel have increased 193, or 16%, in number in five years in the Canadian schools, whereas there has been an increase of 300 or 10% in United States schools, according to comparison of the current study with that of five years ago.

MEDICAL STUDENTS

ENROLLMENTS

In 1958-1959 the number of students enrolled in the 85 medical schools in the United States was again larger than in previous years. The total first year class was 8,128, as compared with 8,030 in 1957-1958. Total enrollment of medical students was 29,614, which was 141 more than in the previous year. As can be noted in table 21, this is the largest total enrollment to date. Complete enrollment data for individual schools is shown in table 1.

Table 1, as well as other tables, includes information about students in the newly developing schools (Seton Hall College of Medicine and Dentistry and University of Florida College of Medicine) which are provisionally approved on the basis of full implementation of the first two years. Also, the figures in table 1 for enrollments by class as well as the total enrollments include the special and part-time students. The numbers of these students are tabulated for each school in the column after total enrollment, although they are distributed in the enrollment figures in the prior columns. A special study was reported last year of the categories of programs setting apart the part-time and special students. Such a study was not repeated in the current year.

Table 21.—*Schools, Students, and Graduates in the Medical and Basic Medical Science Schools in the United States, 1931-1959*

	Schools	1st Year	2nd Year	3rd Year	4th Year	Total	Graduates
1930-1931	76	6,456	5,538	5,080	4,908	21,982	4,735
1931-1932	76	6,260	5,462	4,932	4,885	22,135	4,936
1932-1933	77	6,426	5,479	5,017	4,948	22,466	4,895
1933-1934	77	6,457	5,571	4,988	4,937	22,799	5,035
1934-1935	77	6,356	5,642	5,142	4,905	22,888	5,101
1935-1936	77	6,605	5,458	5,230	5,020	22,564	5,183
1936-1937	77	5,910	5,269	5,140	5,158	22,095	5,377
1937-1938	77	5,791	5,225	4,986	5,036	21,587	5,194
1938-1939	77	5,764	5,160	4,947	4,921	21,302	5,089
1939-1940	77	5,794	5,177	4,921	4,894	21,271	5,097
1940-1941	77	5,837	5,254	4,969	4,849	21,379	5,275
1941-1942	77	6,218	5,406	5,087	4,942	22,031	5,163
1942-1943	76	6,425	5,828	5,278	5,100	22,631	5,223
1943-1944	77	6,561	6,071	5,640	5,257	23,529	5,134
1944 (2nd session)	77	6,648	6,140	6,084	5,794	24,666	5,169
1944-1945	77	6,523	5,979	5,700	5,826	24,028	5,136
1945-1946	77	6,060	5,750	5,751	5,655	23,216	5,826
1946-1947	77	6,564	5,575	5,767	5,994	23,900	6,389
1947-1948	77	6,487	5,758	5,154	5,340	22,739	5,543
1948-1949	78	6,688	6,194	5,702	5,086	23,670	5,094
1949-1950	79	7,042	6,344	6,079	5,638	25,103	5,553
1950-1951	79	7,177	6,690	6,263	6,056	26,186	6,135
1951-1952	79	7,436	6,864	6,577	6,195	27,076	6,080
1952-1953	79	7,425	7,063	6,725	6,475	27,688	6,668
1953-1954	80	7,449	7,068	6,983	6,727	28,227	6,861
1954-1955	81	7,576	7,104	6,957	6,946	28,583	6,977
1955-1956	82	7,686	7,174	6,893	6,886	28,639	6,845
1956-1957	85*	8,014	7,259	7,023	6,834	29,130	6,796
1957-1958	85*	8,030	7,504	7,051	6,888	29,473	6,861
1958-1959	85†	8,128	7,432	7,182	6,872	29,614	6,860

* Includes schools in development.
† Includes schools provisionally approved.

The median total enrollment of all 85 schools in 1958-1959 was 330, and the average total enrollment was 348. If the group of 79 schools having students in all four years is considered, the median total enrollment was 337 and the average total enrollment was 367. Although the average four years ago (1954-1955) was 375 students, the median then was 334+, not a significant change.

The same four schools, as was the case in the previous year, each had a total enrollment greater than 600 (Michigan, Illinois, Jefferson, and Tennessee). Two of them admitted more than 200 students to the 1958-1959 entering class (Illinois 201 and Tennessee 202). Three of the four largest schools admitted fewer students to the 1958-1959 entering class as compared to the previous year: Michigan 9 fewer, Jefferson 3 fewer, and Tennessee 18 fewer. However, the University of Illinois enrolled 11 more students in the 1958-1959 first-year class than was the case last year. In addition to the foregoing, there were three state schools having first year enrollments greater than 150 (Indiana, New York at Brooklyn, and Ohio). This is two fewer than in 1957-1958.

The total entering class (8,128) was the largest to date enrolled in approved medical schools in the United States, as table 21 portrays. There was not the sharp increase over the previous year such as occurred in 1956-1957, however, because unlike that year when the classes in three newly developing schools were included, no additional classes appear in the 1958-1959 figures. Entering class sizes increased in 35 schools, were unchanged in 24, and decreased in 26. A substantial increase occurred at Wayne State University College of Medicine. The addition of 50 students the size of the entering class increased by 67%. This increase was planned for during the past three years during which the faculty and budget had a comparable augmentation to make the larger class size possible. Three other schools had significant increases in first year enrollments: University of California, up 28%; University of California at Los Angeles, up 12%; and University of Wisconsin, up 12%. The only major decrease in entering enrollment was in the University of Tennessee medical school, with 18 fewer students, down 8%.

The median entering class numbered 86, the same as that in 1957-1958. The average first year class was 95.6, comparable to 94.5 the year previously.

Table 22, prepared by the Association of American Medical Colleges, lists by schools the number of applicants and applications to each of the schools for the 1958-1959 class. It should be noted that, even though the numbers of men and women listed as applying to each school are individual applicants to each school, the over-all totals of these columns enumerate applications, not applicants. A total of 59,102 applications were filed by 15,170 persons, or an average of 3.9 applications made by each prospective medical student. Inspection of table 22 reveals that the applicant to class place ratio varies tenfold among the schools, ranging from 1.7 to 17:1.

The number of applicants decreased by 621, about 4% less than a year ago. This coupled with the increased size of the first year class, the over-all applicant to class place ratio was thus 1.86:1, the first year in more than a decade that it has fallen below 1.92. Table 23 presents comparable figures for entering class, applicants, and ratio during the past 11 years. The post World War II unusual flood of applicants had disappeared by 1953-1954,

TABLE 22.—*Number of Applicants and Completed Applications by Medical School for Class First Entering 1958-1959**

	Size of Freshmen Class	No. of Applications			Total Applications Filed by Applicants to Each School	Av. No. of Applications per Applicant
		Men	Women	Total		
Medical College of Alabama	81	308	18	326	1,794	5.5
University of Arkansas School of Medicine	95	172	7	179	292	1.6
College of Medical Evangelists	114	175	16	191	532	2.8
University of California School of Medicine, Los Angeles	56	548	46	594	4,610	7.8
University of Southern California School of Medicine, Los Angeles	68	642	45	687	5,726	8.3
Stanford University School of Medicine	61	610	50	660	5,339	8.1
University of California School of Medicine, San Francisco	101	572	45	617	4,555	7.4
University of Colorado School of Medicine	86	207	10	217	667	3.1
Yale University School of Medicine	81	984	73	1,057	8,957	8.5
Georgetown University School of Medicine	112	1,107	58	1,165	10,216	8.8
George Washington University School of Medicine	101	1,209	62	1,271	11,485	9.0
Howard University College of Medicine	105	613	49	662	3,396	5.1
University of Miami School of Medicine	75	225	12	237	1,276	5.4
University of Florida College of Medicine	50	304	14	318	2,369	7.4
Emory University School of Medicine	74	665	28	693	4,679	6.8
Medical College of Georgia	102	250	12	262	631	2.4
Chicago Medical School	72	981	18	999	10,059	10.1
Northwestern University Medical School	132	1,314	69	1,383	10,391	7.5
Stritch School of Medicine of Loyola University	88	711	23	734	5,005	6.8
University of Chicago, The School of Medicine	73	938	52	990	8,628	8.7
University of Illinois College of Medicine	201	630	31	661	2,734	4.1
Indiana University School of Medicine	160	479	33	512	2,496	4.9
State University of Iowa College of Medicine	120	195	4	199	462	2.3
University of Kansas School of Medicine	98	286	20	306	1,750	5.7
University of Louisville School of Medicine	100	320	10	330	1,588	4.8
Louisiana State University School of Medicine	129	256	19	275	673	2.4
Tulane University School of Medicine	134	1,041	44	1,085	7,455	6.9
Johns Hopkins University School of Medicine	74	923	77	1,000	8,165	8.2
University of Maryland School of Medicine and College of Physicians and Surgeons	100	325	12	337	2,707	8.0
Boston University School of Medicine	74	1,102	81	1,183	11,495	9.7
Harvard Medical School	114	1,179	95	1,274	9,243	7.3
Tufts University School of Medicine	114	942	59	1,001	9,606	9.6
University of Michigan Medical School	197	561	42	603	2,465	4.1
Wayne State University College of Medicine	125	294	20	314	1,117	3.6
University of Minnesota Medical School	139	286	21	307	1,158	3.8
University of Mississippi School of Medicine	78	243	9	252	1,056	4.2
University of Missouri School of Medicine	76	196	11	207	652	3.1
Saint Louis University School of Medicine	126	1,109	39	1,148	8,864	7.7
Washington University School of Medicine	86	1,353	61	1,414	10,767	7.6
Creighton University School of Medicine	77	1,038	31	1,069	8,724	8.2
University of Nebraska College of Medicine	81	199	5	204	727	3.6
Dartmouth Medical School	24	321	3	324	3,013	9.3
Seton Hall College of Medicine and Dentistry	80	1,188	71	1,259	11,113	8.8
Albany Medical College of Union University	65	1,058	53	1,111	10,806	9.7
University of Buffalo School of Medicine	88	666	28	694	6,960	10.0
Albert Einstein College of Medicine of Yeshiva University	96	881	55	936	9,640	10.3
Columbia University College of Physicians and Surgeons	120	1,223	118	1,341	10,877	8.1
Cornell University Medical College	86	1,061	108	1,169	10,207	8.7
New York Medical College, Flower and Fifth Avenue Hospitals	127	1,579	100	1,679	15,360	9.1
New York University College of Medicine	132	1,248	124	1,372	13,398	9.8
State University of New York Downstate Medical Center, New York City	154	1,134	84	1,218	11,375	9.3
University of Rochester School of Medicine and Dentistry	69	1,035	49	1,084	10,642	9.8
State University of New York Upstate Medical Center, Syracuse	87	873	41	914	8,642	9.5
University of North Carolina School of Medicine	70	313	14	327	1,788	5.5
Duke University School of Medicine	79	888	32	920	7,654	8.3
Bowman Gray School of Medicine of Wake Forest College	55	821	39	860	6,879	8.0
University of North Dakota School of Medicine	41	80	2	82	322	3.9
University of Cincinnati College of Medicine	92	963	34	997	8,031	8.1
Western Reserve University School of Medicine	78	1,272	81	1,353	10,725	7.9
Ohio State University College of Medicine	151	499	26	525	2,341	4.5
University of Oklahoma School of Medicine	100	238	12	250	1,147	4.6
University of Oregon Medical School	80	435	24	459	3,144	6.8
Hahnemann Medical College and Hospital of Philadelphia	109	323	17	340	2,325	6.8
Jefferson Medical College of Philadelphia	175	1,599	...	1,599	11,206	7.0
Temple University School of Medicine	136	1,182	62	1,244	9,890	8.0
University of Pennsylvania School of Medicine	126	1,576	93	1,669	13,416	8.0
Woman's Medical College of Pennsylvania	51	...	207	207	1,202	5.8
University of Pittsburgh School of Medicine	101	626	44	670	5,125	7.6
University of Puerto Rico School of Medicine	55	105	18	123	385	3.1
Medical College of South Carolina	80	196	9	205	480	2.3
State University of South Dakota School of Medicine	44	292	5	297	2,430	8.2
University of Tennessee College of Medicine	202	731	28	759	2,371	3.1
Meharry Medical College	74	335	27	362	1,512	4.2
Vanderbilt University School of Medicine	52	679	24	703	6,205	8.8
University of Texas Southwestern Medical School	101	480	25	505	1,620	3.2
University of Texas Medical Branch	143	509	25	534	1,739	3.3
Baylor University College of Medicine	84	918	43	961	7,004	7.3
University of Utah School of Medicine	57	309	3	312	1,879	6.0
University of Vermont College of Medicine	51	303	17	320	2,631	8.2
University of Virginia School of Medicine	76	535	30	565	4,017	7.1
Medical College of Virginia	85	384	21	405	2,387	5.9
University of Washington School of Medicine	75	400	23	423	2,681	6.3
West Virginia University School of Medicine	41	109	5	114	351	3.1
University of Wisconsin Medical School	101	192	17	209	698	3.3
Marquette University School of Medicine	105	752	27	779	5,857	7.5
TOTAL	8,128	55,803	3,299	59,102*		3.9

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* Total number of applications, not applicants, filed to all medical schools. Total number of individuals applying for entrance to Fall 1958 class was 15,170. Average applications per applicant were 3.9.

From the upcoming "Study of Applicants," Association of American Medical Colleges.

with relatively little change until 1958-1959. This may not indicate a continuing downward trend any more than the relative rise during the three years beginning 1954-1955 indicated a continuing upward trend in proportion of applicants to places.

TABLE 23.—*Number of Applicants to Medical Schools, 1948-1959*

Year	Individual Applicants, No.	Ratio of First-Year Class to Total Applicants
1948-1949	24,242	3.62
1949-1950	24,434	3.47
1950-1951	22,279	3.10
1951-1952	19,920	2.68
1952-1953	16,763	2.26
1953-1954	14,678	1.97
1954-1955	14,538	1.92
1955-1956	14,937	1.94
1956-1957	15,918	1.99
1957-1958	15,791	1.97
1958-1959	15,170	1.86

It is a matter deserving of study in order that any sharp diminution in applicants that may be significant will be noted early enough to permit additional career guidance efforts to be directed toward highly capable young people.

The 12 Canadian medical schools had in 1958-1959 a slightly smaller total enrollment in the four medical school years than was reported a year ago. Though five schools had increased enrollments (Toronto and Montreal had the largest increases, each about 3.5%), seven had decreased total enrollments, of which the more significant changes were Saskatchewan, down 7%; Laval, down 5%; McGill and Manitoba, each down about 3.5%. Comparative data are presented in table 24 for enrollments in previous years in the Canadian medical schools. The median enrollment in 1958-1959 was 227 students and the average 306, nearly identical with the figures reported one year ago. Data on the applicants and applications to Canadian schools were not available.

GEOGRAPHICAL SOURCE OF ENTERING STUDENTS

The residence of students at the time of their enrollment in the medical schools in the United States is shown in table 25 based on the 1958-1959 enrollment data.

Of all first-year medical students, more than one-third (37%) came from five states (New York, Pennsylvania, California, Ohio, and Illinois). As was the case for the past three years, 41% of the entering class came from six states (those above and Texas) and their 32 schools enrolled 40% of the class. Michigan contributed an equal number of students as did Texas (342). Those seven states originated about 46% of the total entering medical class in 1958-1959, and the 34 medical schools in the seven states enrolled 44% of the total first-year class. Forty per cent of all medical schools in the United States are located in the same seven states.

There were fewer than 20 first-year medical students from each of seven states (Alaska, Delaware, Maine, Nevada, New Mexico, Vermont, and Wyoming) and fewer than 30 from two other states (New Hampshire and Rhode Island). Of these nine states, only New Hampshire and Vermont have medical schools. The 74 students from the seven states originating the fewest students and the 43 students from the other two states together comprise only 1.4% of the total first-year class, 83 students and 1.0% less than in the 1957-1958 academic year.

In table 26 are listed the states in ascending order according to the number of enrolled first-year medical students per 100,000 population. As was the case in the previous two academic years, the seven states originating the largest number of first-year students are distributed throughout the list. With the sole exception of Nevada, the other eight states having the smallest number of first-year students enrolled in medical schools had relative to the population fewer students than the median number (4.45). As compared with last year, Vermont slipped from 5.0 to 3.0 and Wyoming from 5.5 to 2.5, on the basis of 14 fewer students from Vermont and 9 fewer from Wyoming. Nevada jumped from 3 students in 1957-1958 to 10 in 1958-1959, changing its ratio from 1.2 to 5.0. Five other states have shown a change in their relation to the median number, three (Idaho, Kentucky, Maryland) having risen from below to above, while Connecticut and Florida have gone from above the median to below. Though others have shown changes in ratio of medical students to population, their position in the rank order has not changed remarkably.

The over-all ratio of students per 100,000 population, excluding members of the armed forces, was 4.6, 0.1 less than in 1957-1958. The number of first-year medical students enrolled in 1958-1959 did not quite keep pace with the total population growth, even though the class was 92 students larger than in the previous year.

TABLE 24.—*Schools, Students, and Graduates in the Medical and Basic Medical Science Schools in Canada, 1948-1959*

	Schools	1st Year	2nd Year	3rd Year	4th Year	Total	Graduates
1948-1949	10	887	765	842	739	3,233	679
1949-1950	10	897	798	761	822	3,278	791
1950-1951	11	960	880	844	805	3,489	858
1951-1952	11	873	891	858	836	3,458	783
1952-1953	11	918	809	865	852	3,444	825
1953-1954	12	982	901	844	916	3,643	896
1954-1955	12	968	903	881	837	3,589	894
1955-1956	12	1,035	883	877	856	3,651	816
1956-1957*	12	1,001	934	855	865	3,655	893
1957-1958	12	1,012	916	928	830	3,686	828
1958-1959	12	986	911	867	904	3,668	859

* The remaining school of the basic medical sciences (Saskatchewan) became a four-year school with students in all years.

There were six schools, all publicly owned, that enrolled as first-year medical students only those resident in the state in which the school is located.

An additional six publicly owned schools each enrolled only one nonresident student, less than 1% of their classes. Four additional publicly owned schools had fewer than 5% nonresidents in their entering classes. A total of 16 publicly owned schools (or 40% of all publicly owned medical schools) each had fewer than 5% of their entering classes composed of students from other states (17 students in all). Table 27 provides information on out-of-state enrollments for 1958-1959 as compared with 1957-1958. A special study of the effect of geographical restrictions on attrition for poor scholarship was published one year ago in the 58th annual report, Medical Education in the United States and Canada.[11]

Because of a change in the manner of collecting information for the 1958-1959 year, the residence of entering students in the 12 Canadian medical schools was not available.

COLLEGE RECORD OF FIRST-YEAR MEDICAL CLASS

Table 28 presents comparative data of the college scholastic record of the entering classes in medicine since 1950-1951. There is no significant change in the past year or, indeed, since 1953-1954. At least two-thirds of the entering classes comprise "B" average students. About one-sixth had college grade averages of "A" and about one-sixth to one-seventh had "C" averages. Four of the 85 schools, privately owned, did not report on the college record of their first-year classes in 1958-1959. In 1958-1959, 27 schools had more than the average proportion (16.0%) of "A" students and 54 schools had a smaller proportion. Sixteen of the 27 schools are privately owned and 11 publicly owned. The range was extremely wide, from 0 to 57% of "A" students in various first-year classes. Only one school had no such students, while four schools had more than 40% of their entering classes consisting of "A" students. Of the 81 schools that reported, 47 had a smaller proportion of "C" average students than the average (14.3%), while 34 schools had a larger proportion. The range was wide; from 0 to 59% of the classes entering various schools were composed of "C" students. Six schools had no students in this category. Five schools had more than 40% of their first-year classes composed of students having "C" college records. All of the five have geographical or other rigorous restrictions on choice of student body from among applicants.

A year ago, in the 58th Annual Report,[11] a special study of the significant relationship of geographical restriction to medical student attrition for academic failure was presented.

It should be pointed out to others than admissions committee members, who already are acutely aware of this, that there are differences among colleges in the relationship of a given grade average to scholastic achievement. For instance, scholastic achievement in one college that is awarded a "B" grade might in another college be given a "C" grade and similarly, though to a lesser degree, in the case of "A" and "B" grades. The scholastic record in college is one factor among many that are considered in the selection of students by medical school faculties.

The college grade averages of students entering the first medical year of the Canadian medical schools in 1958-1959 is also presented in table 28. There is a somewhat smaller proportion of students having "B" college records, and a larger proportion of the entering class having "A" as well as "C" records than in United States schools. There was less variation among the Canadian schools in the proportions of students having different college records than was the case in United States schools. Seven Canadian schools had a greater proportion than the average (17.9%) of entering students having "A" college records. The range, however, for all 12 schools is 7.9 to 38.2%. Only one school had more than 30% of the class composed of "A" students, although three additional schools had 25% or more such students in their entering medical classes. Six schools had less than the average proportion (23.8%) of "C" students. The range for the 12 schools of proportions of "C" students was 3.3 to 46%. Only one school had more than 40% of the class composed of such students.

PREPROFESSIONAL ATTAINMENTS OF THE ENTERING CLASS

Table 29 presents by school the preprofessional educational attainments of the 1958-1959 entering class. Table 30 provides comparative data for previous years with the 1958-1959 year. It is apparent that the trend toward longer college education prior to entering medical school is a continuing one if one considers together those who have completed four years of college and those students having a college degree. Twenty-two years ago, 61% of first-year medical students were in that category, whereas in 1958-1959 80.4% of entering medical students have either completed four years of college or have earned one (or more) college degrees. As table 30 shows, there has been an increase of 5.5% of the class in this group in the past five years. About four-fifths of the first-year class have had such attainments during the last two years. It is likely that as such schools as Stanford, Boston University, and Johns Hopkins implement their new programs interdigitating college and medical school education, this trend will be reversed when a sufficient number of students are involved. This will also depend on whether, in relation to such innovations in medical education, the definition of a first-year medical student is altered from its present sense of a student who is four years removed from the M.D. degree.

TABLE 25.—*Geographical Source of Entering Students in Medical*

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21
	School	Alabama	Alaska	Arizona	Arkansas	California	Colorado	Connecticut	Delaware	District of Columbia	Florida	Georgia	Hawaii	Idaho	Illinois	Indiana	Iowa	Kansas	Kentucky	Louisiana	Maine	Maryland
1	Medical College of Alabama	72	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..
2	University of Arkansas School of Medicine	..	..	..	95	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
3	College of Medical Evangelists	..	..	2	..	42	1	..	..	..	..	1	..	..	1	..	..	..	..	2	..	3
4	University of California School of Medicine, Los Angeles	..	..	4	..	51	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
5	University of Southern California School of Medicine	..	..	1	..	62	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..
6	Stanford University School of Medicine	..	..	3	..	48	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..
7	University of California School of Medicine, San Francisco	..	..	3	..	97	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..
8	University of Colorado School of Medicine	..	1	1	..	..	73	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
9	Yale University School of Medicine	..	..	2	..	4	1	13	1	..	..	..	1	..	2	..	1	..	1	..	1	3
10	Georgetown University School of Medicine	..	..	..	..	1	..	5	..	14	1	1	..	..	..	..	..	1	..	..	1	3
11	George Washington University School of Medicine	..	..	..	..	13	..	..	1	15	1	..	..	7	1	3	..	..	..	..	..	5
12	Howard University College of Medicine	2	1	3	1	5	..	..	1	14	4	2	..	..	6	1	1	..	..	2	..	3
13	University of Miami School of Medicine	..	..	..	..	..	..	..	..	..	71	..	..	..	..	..	..	..	..	..	..	..
14	University of Florida College of Medicine	..	..	..	..	..	..	1	..	..	42	2	..	..	..	..	..	..	..	..	..	..
15	Emory University School of Medicine	4	..	..	..	..	..	1	..	..	15	41	..	..	..	1	..	..	..	..	..	..
16	Medical College of Georgia	..	..	..	..	..	..	..	..	..	..	101	..	..	..	..	..	..	..	..	..	..
17	Chicago Medical School	..	..	..	..	1	..	1	..	2	1	..	..	..	8	..	..	..	..	..	..	..
18	Northwestern University Medical School	..	..	..	..	5	2	1	..	..	1	..	1	1	53	5	3	1	2	1	..	1
19	Stritch School of Medicine of Loyola University	..	..	..	..	5	..	1	..	..	..	..	..	..	37	3	..	..	1	..	..	1
20	University of Chicago, The School of Medicine	..	..	..	..	6	..	..	..	1	..	1	..	..	34	4	..	..	..	..	..	..
21	University of Illinois College of Medicine	..	..	..	..	1	..	..	..	..	..	..	..	..	200	..	..	..	..	..	..	..
22	Indiana University School of Medicine	..	..	..	..	..	..	..	..	..	1	..	1	..	2	148	..	1	1	..	..	..
23	State University of Iowa College of Medicine	..	..	..	..	..	..	..	..	..	1	..	..	..	5	..	112	..	..	..	..	..
24	University of Kansas School of Medicine	..	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	83	..	..	..	..
25	University of Louisville School of Medicine	..	..	..	..	1	..	..	..	..	..	..	..	..	..	3	..	..	87	..	..	..
26	Louisiana State University School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	128	..	..
27	Tulane University School of Medicine	13	..	6	3	1	..	..	..	..	7	1	2	..	2	1	..	..	3	30	..	..
28	Johns Hopkins University School of Medicine	1	..	..	1	1	1	2	..	1	2	1	..	..	5	2	..	..	2	..	..	13
29	University of Maryland School of Medicine	..	..	..	..	1	..	1	..	1	..	..	..	..	1	..	..	..	..	1	..	79
30	Boston University School of Medicine	..	..	..	..	6	..	1	..	1	..	..	2	..	..	..	..	..	..	..	1	1
31	Harvard Medical School	..	..	..	..	4	3	3	1	..	1	1	1	..	5	3	..	..	..	..	1	1
32	Tufts University	..	..	..	..	..	..	16	1	..	..	..	..	..	..	..	..	..	..	..	1	1
33	University of Mi	..	..	..	..	2	2	1	..	..	1	..	1	1	2	..	1	..	..	..	..	..
34	Wayne State Uni	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
35	University of Minnesota Medical School	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..
36	University of Mississippi School of Medicine	..	..	..	..	..	..	..	..	..	2	..	..	..	1	..	..	..	..	..	..	..
37	University of Missouri School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
38	Saint Louis University School of Medicine	1	..	2	1	20	2	3	..	..	..	..	2	1	11	3	3	2	2	1	..	..
39	Washington University School of Medicine	..	..	2	..	7	1	..	..	1	4	..	..	3	5	1	1	1	..	..	..	2
40	Creighton University School of Medicine	..	..	1	..	15	2	1	..	..	..	..	1	1	1	..	12	1	..	..	..	..
41	University of Nebraska College of Medicine	..	..	..	..	1	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
42	Dartmouth Medical School	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	1	..	..	..
43	Seton Hall College	..	..	..	..	..	..	5	1	..	..	..	..	..	..	..	..	..	..	..	..	..
44	Albany Medical Coll	..	..	..	..	2	..	2	..	1	..	..	..	..	..	1	..	..	..	..	..	1
45	University of Buffalo School of Medicine	..	..	..	..	2	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..
46	Albert Einstein College of Medicine of Yeshiva University	..	..	..	..	1	1	2	..	..	..	..	..	..	..	..	..	..	..	..	..	1
47	Columbia University College of Physicians and Surgeons	..	..	..	..	2	..	4	..	3	1	..	..	..	3	1	..	..	1	1	..	1
48	Cornell University Medical College	..	..	2	..	6	..	1	1	1	1	1	..	1	1	1	..	..	1	..	..	..
49	New York Medical College, Flower and Fifth Avenue Hospitals	..	..	..	..	3	..	10	1	..	..	1	..	..	1	..	..	..	..	..	..	..
50	New York University College of Medicine	..	..	..	..	1	..	2	..	..	..	..	..	..	..	..	..	..	..	..	3	..
51	State University of New York Downstate Medical Center, New York City	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..
52	University o	..	..	..	..	1	..	1	..	1	..	..	1	..	1	..	..	..	..	..	..	..
53	State Univer	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..
54	University of North Carolina School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
55	Duke University School of Medicine	1	..	..	..	..	1	..	..	..	5	4	..	..	..	1	..	1	2	..	..	1
56	Bowman Gray School of Medicine of Wake Forest College	..	..	..	..	1	..	..	..	..	..	2	..	..	..	..	..	..	3	..	..	..
57	University of North Dakota School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
58	University of Cincinnati College of Medicine	..	..	..	..	1	..	..	..	..	..	..	..	..	1	2	..	..	6	..	..	..
59	Western Reserve University School of Medicine	..	..	..	..	3	3	2	..	1	2	..	..	..	4	1	..	..	..	..	..	1
60	Ohio State University College of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..
61	University of Oklahoma School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
62	University of Oregon Medical School	..	1	1	..	3	..	..	..	..	..	..	1	2	..	..	1	..	..	..	..	..
63	Hahnemann Medical College and Hospital of Philadelphia	..	..	..	..	2	..	1	..	..	..	..	2	..	1	..	..	..	..	..	..	1
64	Jefferson Medical College of Philadelphia	..	..	1	..	..	..	1	3	1	1	..	1	..	..	..	1	..	..	..	..	..
65	Temple University School of Medicine	1	..	..	..	..	..	..	2	1	1	..	..	1	1	..	..	..	..	..	..	1
66	University of Pennsylvania School of Medicine	..	..	..	..	2	1	..	2	1	..	..	..	..	..	1	..	..	2	..	..	2
67	Woman's Medical College of Pennsylvania	..	..	..	..	1	..	..	1	..	..	..	..	..	1	1	..	..	1	..	..	..
68	University of Pittsburgh School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	1	..
69	University of Puerto Rico School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
70	Medical College of South Carolina	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
71	State University of South Dakota School of Medicine	..	..	1	..	1	1	..	..	..	..	..	..	1	1	..	8	..	..	..	..	..
72	University of Tennessee College of Medicine	3	..	4	6	..	..	..	..	..	3	2	..	..	1	..	..	..	5	1	..	..
73	Meharry Medical College	6	..	..	1	1	..	1	..	..	3	5	..	..	3	..	..	..	1	5	..	2
74	Vanderbilt University School of Medicine	3	..	..	3	1	..	..	..	..	1	3	..	..	..	..	..	..	15	..	..	..
75	University of Texas Southwestern Medical School	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
76	University of Texas Medical Branch, Galveston	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
77	Baylor University College of Medicine	..	..	1	1	12	1	..	..	..	1	..	1	..	2	..	..	1	..	..	..	..
78	University of Utah School of Medicine	..	..	3	..	2	..	..	..	..	..	..	..	7	1	..	..	..	..	..	..	..
79	University of Vermont College of Medicine	..	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	5	..
80	University of Virginia School of Medicine	..	..	..	..	1	..	1	..	2	..	1	..	..	..	..	..	..	..	..	..	3
81	Medical College of Virginia	..	..	..	..	..	..	2	..	..	..	..	..	..	..	1	..	..	..	..	..	1
82	University of Washington School of Medicine	..	1	..	..	1	..	..	..	..	..	..	1	3	1	..	..	..	..	..	..	..
83	West Virginia University School of Medicine	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
84	University of Wisconsin Medical School	1	..	..	..	..	..	1	..	..	..	..	..	..	..	1	1	..	..	..	..	..
85	Marquette University School of Medicine	..	..	1	..	14	..	..	..	..	..	..	1	..	6	..	2	..	..	..	..	..
	Totals	108	4	45	112	464	97	93	18	62	174	173	23	30	413	190	148	93	137	172	14	131
	Marginal No.	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21

and Basic Medical Science Schools of the United States, 1958-1959

22 Massachusetts	23 Michigan	24 Minnesota	25 Mississippi	26 Missouri	27 Montana	28 Nebraska	29 Nevada	30 New Hampshire	31 New Jersey	32 New Mexico	33 New York	34 North Carolina	35 North Dakota	36 Ohio	37 Oklahoma	38 Oregon	39 Pennsylvania	40 Puerto Rico	41 Rhode Island	42 South Carolina	43 South Dakota	44 Tennessee	45 Texas	46 Utah	47 Vermont	48 Virginia	49 Washington	50 West Virginia	51 Wisconsin	52 Wyoming	53 Guam, Panama and Others	54 Canada	55 Foreign	56 Home State	57 Out of State	58 Totals	Marginal Number
1	1	..	..	..	..	..	..	..	1	..	2	..	..	..	..	..	1	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	72	9	81	1
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	95	0	95	2
1	2	1	1	..	..	2	2	..	..	..	4	..	..	5	3	4	..	1	..	..	1	2	4	..	..	1	12	..	1	..	..	3	12	42	72	114	3
1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	51	5	56	4
..	..	..	..	..	..	..	2	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	62	6	68	5
..	..	..	1	..	..	1	..	..	1	1	1	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	48	13	61	6
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	97	4	101	7
..	..	..	..	..	..	..	..	..	..	8	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	..	..	73	13	86	8
13	1	..	..	1	..	..	..	1	5	..	18	..	..	3	1	1	5	..	1	..	..	..	1	..	..	..	..	..	..	..	..	..	..	13	68	81	9
10	2	..	..	..	..	..	..	..	19	..	30	..	..	7	..	..	7	1	3	..	..	..	..	..	..	3	1	..	..	..	..	..	2	14	98	112	10
3	1	1	..	..	1	1	1	..	8	1	12	..	..	1	..	1	10	..	..	..	..	..	..	1	..	5	2	1	1	..	..	..	..	15	86	101	11
2	1	..	1	3	..	..	..	..	4	..	15	..	..	2	..	..	10	..	..	4	..	2	..	..	..	9	..	..	..	..	..	..	10	14	91	105	12
..	..	..	..	..	..	..	..	..	..	1	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	71	4	75	13
..	..	..	..	..	..	..	..	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	1	42	8	50	14
..	..	..	..	..	..	..	..	..	..	..	3	..	..	1	..	..	..	..	..	2	..	4	1	..	..	1	..	..	..	..	..	..	..	41	33	74	15
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	101	1	102	16
2	..	..	..	..	..	..	..	..	7	..	47	..	..	1	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	8	64	72	17
1	5	4	..	4	..	2	..	..	4	2	7	..	..	11	..	..	2	..	..	..	1	..	..	1	..	..	1	1	5	1	..	1	2	53	79	132	18
2	4	..	..	2	2	..	..	..	2	..	8	..	..	11	..	1	3	..	..	..	..	..	..	..	..	..	..	..	2	..	..	1	2	37	51	88	19
..	3	2	..	1	..	2	..	..	3	..	4	..	..	6	1	..	1	..	..	..	1	1	..	..	..	..	..	1	1	..	..	..	..	34	39	73	20
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	200	1	201	21
..	1	..	..	..	..	..	..	..	..	..	1	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	..	1	148	12	160	22
..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	112	8	120	23
..	..	..	..	10	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	83	15	98	24
..	..	..	..	..	..	..	..	..	1	..	4	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	1	87	13	100	25
..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	128	1	129	26
..	..	..	18	3	..	..	..	..	4	1	5	1	..	2	1	..	..	..	..	2	..	1	16	..	..	1	..	1	..	..	..	..	9	30	104	134	27
2	1	..	..	..	..	1	1	1	4	..	16	2	..	4	..	..	1	..	..	1	..	3	1	..	..	1	..	1	1	..	..	..	1	13	61	74	28
1	..	..	..	..	1	..	..	1	2	..	1	..	..	1	..	1	5	..	1	..	..	..	..	1	..	..	1	..	..	..	..	..	..	79	21	100	29
41	..	2	..	..	..	..	..	..	3	..	10	..	..	2	..	..	1	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	2	41	33	74	30
20	3	..	1	..	1	1	..	..	3	..	32	4	..	8	1	..	9	..	1	..	1	..	..	..	..	1	1	1	1	..	..	..	1	20	94	114	31
51	..	..	..	2	..	..	..	4	3	..	21	..	..	9	..	..	1	..	4	..	..	..	..	..	..	..	..	..	..	..	..	..	..	51	63	114	32
..	169	..	..	..	..	..	1	..	1	..	5	..	..	7	..	..	..	1	..	..	..	..	1	..	..	..	..	..	..	..	..	..	1	169	28	197	33
..	124	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	124	1	125	34
..	..	136	..	..	..	..	..	..	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	136	3	139	35
..	..	..	74	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	74	4	78	36
..	..	..	..	76	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	76	0	76	37
4	2	3	..	18	3	..	1	1	3	..	7	..	1	10	1	..	1	..	..	..	..	1	3	1	..	..	3	..	2	..	..	..	7	18	108	126	38
1	2	..	2	23	..	1	..	..	1	1	4	1	..	4	2	3	1	..	..	..	..	1	9	..	..	..	1	..	..	1	..	..	..	23	63	86	39
..	..	3	..	1	2	13	1	..	2	..	6	..	..	2	..	1	..	..	2	..	6	..	..	..	..	..	..	..	1	..	..	..	2	13	64	77	40
..	..	..	..	1	..	75	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	1	..	..	..	..	..	..	75	6	81	41
1	1	2	..	..	1	..	..	..	4	..	7	1	..	2	..	..	2	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	0	24	24	42
4	..	..	..	..	..	..	..	..	44	..	23	..	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	44	36	80	43
1	..	..	..	..	..	..	..	..	10	..	41	..	..	2	..	..	..	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	41	24	65	44
..	..	..	..	..	..	..	..	..	2	..	77	..	..	3	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	77	11	88	45
1	..	..	..	..	..	..	..	..	5	..	80	1	..	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	80	16	96	46
3	..	..	..	2	..	..	..	..	17	..	57	..	..	11	..	..	7	..	..	..	..	1	..	..	..	..	1	..	3	..	..	..	1	57	63	120	47
..	1	..	..	..	..	1	6	..	12	..	41	..	..	8	..	..	2	..	..	..	..	..	2	..	..	1	..	..	1	..	..	..	..	41	45	86	48
14	..	1	..	..	..	..	..	..	21	..	67	..	..	1	..	..	3	..	2	..	..	..	..	..	..	..	..	..	..	..	..	..	..	67	60	127	49
4	..	..	..	..	..	..	..	..	18	..	96	..	..	3	1	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	96	36	132	50
2	..	..	..	..	..	..	..	..	5	..	143	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	143	11	154	51
2	1	..	..	..	..	..	..	..	4	..	44	..	..	6	..	1	1	..	..	..	..	..	1	..	..	..	..	..	..	3	..	..	1	44	25	69	52
2	2	..	..	..	..	..	..	..	5	..	77	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	77	10	87	53
1	..	..	..	..	..	..	..	..	..	..	..	69	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	69	1	70	54
3	1	..	..	..	..	..	..	..	5	..	9	23	..	2	..	..	2	2	..	4	..	1	3	..	..	4	..	3	1	..	..	..	..	23	56	79	55
..	1	..	..	..	..	..	..	..	1	..	3	32	..	..	..	..	..	..	1	1	..	1	..	1	..	2	..	2	1	..	..	..	3	32	23	55	56
..	..	2	..	..	4	..	..	..	..	..	..	..	34	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	34	7	41	57
1	..	..	..	..	1	..	..	..	..	..	2	..	..	72	..	..	4	..	..	..	..	..	..	1	..	..	..	..	1	..	..	..	..	72	20	92	58
2	4	1	..	..	..	..	..	..	..	..	6	..	..	42	1	..	1	..	1	..	..	..	..	..	..	..	..	1	..	..	..	..	2	42	36	78	59
..	..	..	..	..	..	..	..	..	..	..	..	..	..	150	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	150	1	151	60
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	100	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	100	0	100	61
..	..	..	..	..	2	..	2	..	..	..	..	..	..	..	..	66	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	66	14	80	62
..	..	..	..	..	..	..	..	..	18	..	..	..	..	2	..	..	79	..	1	..	..	..	..	..	..	..	..	..	1	..	..	..	1	79	30	109	63
1	..	..	..	..	..	..	..	..	25	..	4	1	..	1	..	..	124	..	1	..	..	..	2	1	..	2	..	3	..	..	..	..	1	124	51	175	64
2	..	..	..	..	..	..	..	..	10	..	3	..	..	2	..	..	108	1	..	..	..	..	..	..	..	1	..	..	..	..	..	..	1	108	28	136	65
1	..	..	..	..	..	..	..	..	9	..	5	2	..	2	1	..	88	..	..	1	..	..	..	1	..	2	..	1	2	..	..	..	..	88	38	126	66
3	..	..	..	..	..	..	..	..	3	..	20	..	..	2	..	1	14	..	..	..	..	..	..	..	..	..	1	..	..	..	1	..	1	14	37	51	67
..	..	..	..	..	..	..	..	..	1	..	7	..	..	6	..	..	83	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	2	83	18	101	68
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	55	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	55	0	55	69
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	80	..	..	..	..	..	..	..	..	..	..	..	..	..	80	0	80	70
..	..	2	..	..	1	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	23	..	..	..	..	..	1	..	2	..	..	..	1	23	21	44	71
..	..	..	5	7	..	..	..	..	..	1	..	6	..	..	5	..	..	..	..	2	..	146	5	..	..	..	..	..	..	..	..	..	..	146	56	202	72
1	2	..	2	1	..	..	..	..	2	..	2	5	..	2	..	..	1	..	..	4	..	7	10	..	..	4	..	..	..	..	..	..	3	7	67	74	73
..	..	..	2	1	..	1	..	..	1	..	2	..	..	3	1	..	..	..	..	1	..	12	1	..	..	..	..	1	..	..	..	..	..	12	40	52	74
..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	1	..	..	..	..	..	..	..	98	1	..	..	..	..	..	..	..	..	..	98	3	101	75
..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	..	..	..	..	..	142	..	..	..	..	..	..	..	..	..	..	142	1	143	76
..	1	2	4	2	..	1	1	..	1	2	..	..	..	1	4	..	..	..	..	..	..	2	40	..	..	1	1	..	..	..	..	..	1	40	44	84	77
..	..	..	..	..	1	..	1	..	1	..	..	..	..	..	..	..	..	..	..	..	..	1	..	38	..	..	1	..	..	1	..	..	..	38	19	57	78
16	..	..	..	..	..	..	..	13	..	..	2	..	..	..	..	..	..	..	1	..	..	..	..	..	11	..	..	..	..	..	..	..	..	11	40	51	79
1	..	..	..	..	..	..	..	..	1	..	7	2	..	..	..	..	1	..	..	1	..	2	..	..	..	49	..	3	..	..	..	..	1	49	27	76	80
1	..	..	..	..	..	..	..	..	..	..	5	..	..	..	..	..	1	..	1	1	..	..	..	..	..	68	..	2	..	..	..	..	2	68	17	85	81
..	1	..	..	..	3	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	64	..	..	..	..	..	..	64	11	75	82
..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..	41	..	..	..	..	..	41	0	41	83
..	..	..	..	..	..	..	..	..	..	..	..	..	..	1	..	..	..	..	..	..	1	..	..	..	..	..	..	..	95	..	..	..	..	95	6	101	84
..	5	1	..	1	..	..	..	..	1	..	7	..	..	10	..	..	2	..	..	..	1	..	..	..	..	..	2	..	49	..	..	..	2	49	56	105	85
223	312	163	112	159	23	104	13	21	309	18	1,108	150	37	435	126	81	601	61	22	104	35	189	312	47	11	157	95	64	172	8	3	5	87	5,552	2,576	8,128	
22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	

The numbers and proportions of all medical schools in the United States having more than 90% of their entering classes comprised of students having college degrees is presented in table 31, with comparable information for previous years.

Table 26.—*Ratio of First-Year Medical Students to State Populations, 1958-1959*

Numbers of Students per 100,000 population* in the Approved, Newly Developing Medical and Basic Medical Science Schools of the United States.	
Maine†	1.5
New Mexico†	2.2
Alaska†	2.4
Wyoming†	2.5
Rhode Island†	2.6
Vermont	3.0
California	3.3
West Virginia	3.3
Alabama	3.4
Montana†	3.4
North Carolina	3.4
Washington	3.5
New Hampshire	3.6
Missouri	3.7
Texas	3.7
Arizona	4.0
Connecticut	4.0
Delaware†	4.0
Florida	4.0
Illinois	4.2
Indiana	4.2
Virginia	4.2
Michigan	4.4
South Carolina	4.4
Wisconsin	4.4
Kansas	4.5
Kentucky	4.5
Maryland	4.5
Georgia	4.6
Idaho†	4.6
Massachusetts	4.6
Oregon	4.6
Ohio	4.7
Minnesota	4.8
Nevada†	5.0
South Dakota	5.1
Iowa	5.2
Mississippi	5.2
New Jersey	5.4
Pennsylvania	5.4
Tennessee	5.5
Utah	5.5
Louisiana	5.6
Oklahoma	5.6
North Dakota	5.7
Colorado	5.8
Arkansas	6.4
New York	6.8
Nebraska	7.2
District of Columbia	7.7
United States‡	4.6

* Estimated July 1, 1958 total population excluding members of the Armed Forces stationed in each area. Current Population Reports, Series P-25, No. 189, November 13, 1958.

† States with no medical school.

‡ Hawaii is not included, because it was admitted to statehood after the 1958-1959 academic year.

There has been no significant change in 1958-1959 as compared to 1957-1958. Almost one-third of all 85 medical schools in the United States have more than 90% of their first-year students with college degrees.

The foregoing applies to the actual attainments of the entering class. Presumably influencing this are the minimum requirements for applicants as submitted by the medical schools to the Association of American Medical Colleges for publication in its guidebook each year.[12] Table 32 compares these requirements for the preceding two years, the 1959-1960 year, and the 1960-1961 year. It is apparent that each year more schools require four years of college or a degree as their minimum stipulated to applicants. There has, however, been relatively little change for applicants to classes beginning in 1959-1960 and 1960-1961. In the requirements recently published for the class to be admitted in the 1960-1961 year, of the 71 schools requiring at least three years of college, 7 prefer four years of college for their applicants. Of the 9 schools requiring four years of college, one school prefers that its applicants have college degrees. Thus, if the preferences stated were strong ones, it might be more accurate to state that 4 schools will in effect require degrees and an additional 17 schools will in effect require four years of college prior to entering medical school. These 21 schools constitute almost one-fourth of all the medical schools in the United States. Fourteen of the 21, or two-thirds, are privately owned medical schools; the remainder are publicly owned.

Of the 12 Canadian medical schools, the stated admission requirements of nine are three years of college (or two years of college after grade 13), although one of these strongly prefers four years of college (or three years after grade 13), while the other three schools require four years of college. The actual preprofessional attainments of the entering classes were not available.

STUDENTS ADMITTED INTO ADVANCED STANDING

A total of 258 students were admitted into advanced standing in 1958-1959 in 56 medical schools in the United State. Of these, 124 were transfer students from two year schools of the basic medical sciences, 97 were from four-year United States medical schools, 30 were from schools outside the United States and Canada, and 7 were from pharmacy or dental or university graduate schools in the United States. Forty-eight were admitted into second-year classes, 207 transferred to third-year classes, and 3 students transferred into fourth-year classes.

Almost one-half (48%) of the admissions into advanced standing were occasioned by students completing the second year in the four schools of basic medical sciences transferring into the third year of four-year medical schools. Two schools took more than one-third (38%) of such students: Medical College of Virginia (26 students) and Harvard (21). The six schools taking an additional one-third of the students from two year schools into the third year were Nebraska (8), Iowa (7), Kansas (7), Northwestern (7), Texas Southwestern (7), and

Pennsylvania (6). Six of these eight schools, excepting Iowa and Nebraska, accounted for 60% of the students from two-year schools in 1958-1959, nearly the same as in the previous year. The remaining 35 students were accepted into third-year classes of 15 other medical schools in the United States. All students graduated from the schools of basic medical sciences were admitted into third-year classes of the 23 four-year medical schools.

TABLE 27.—*Out-of-State Enrollments of Entering Medical School Class*

	1957-1958					1958-1959				
	Number of Schools			Number of Non-Resident Students Taken into Publicly Owned Schools		Number of Schools			Number of Non-Resident Students Taken into Publicly Owned Schools	
% of Class Non-Resident	Privately Owned	Publicly Owned				Privately Owned	Publicly Owned			
0	0	7	25 Schools	0	79 Students	0	6	23 Schools	0	69 Students
<5	1	11		25		0	10		17	
5-10	1	7		64		2	7		52	
10-20	6	7		70		4	10		190	
Total	8	32		159		6	33		259	

The 48 students admitted to advanced standing into second-year classes of 33 medical schools consisted of 13 foreign students admitted by 11 schools, 27 from United States medical schools, and 8 from graduate or dental schools in the United States.

Sixteen of the transfer students from medical schools outside the United States and Canada were admitted into third-year classes of nine medical schools, and one foreign student was admitted into a fourth-year class.

ATTRITION OF MEDICAL STUDENTS

There has been a change in the method of securing attrition data for the 1958-1959 year as compared with previous years. Previously, questions in the annual questionnaire to medical schools included request for numbers of students leaving medical school for poor scholarship and numbers leaving for other reasons, although in good academic standing. However, for the 1958-1959 year, attrition data were secured from the change of status reports received throughout the year from medical schools in the United States. Decisions regarding the students to include in attrition data and who to omit (such as those withdrawing for a year from medical school for advanced study) were made in a single office rather than in 85 medical school offices. Whether the data are entirely comparable with previous years is thus uncertain.

The information on student loss to medicine is presented in table 33. Included are those who withdrew or were dismissed because of poor academic standing and those who withdrew or were dismissed from medical school for other reasons. Not included in the attrition figures are students withdrawing for special study or research, students who transferred to another medical school, and students who changed their status from full to part time.

There appears to be little significant change as compared with the 1957-1958 academic year. If one compares attrition due to poor scholarship for the years 1954-1955 to 1957-1958 inclusive, there appears to be a slight increase each year, predominantly in the freshman and sophomore classes. The 1958-1959 figures appear to interrupt this trend. It is possible that students were included in attrition data previously that were not included in the 1958-1959 year, so that a different base line may have been introduced for the current data. With similar reservations regarding comparability of data, there was a slight increase in the proportion of first year students in good academic standing withdrawing or dismissed for other reasons. This almost exactly offsets the decline in proportion of students dismissed for poor academic standing so that the over-all attrition was almost the same for 1958-1959 (3.4%) as for 1957-1958 (3.3%).

As was the case in previous years, in 1958-1959 about two-thirds (68%) of all student losses were in the first-year class. Of these losses, 63% were due to failure or withdrawal in poor academic standing. The second-year class in 1958-1959 had 59% of its losses from this cause. In the third-year and fourth-year classes, 27% of the students lost to medicine either failed or withdrew in poor academic standing.

The fact that 73% of the 108 students lost to medicine in their third and fourth years were for nonacademic reasons should occasion special concern. One possible cause might be financial. It is hoped

TABLE 28.—*Comparative Analysis of College Records of First-Year Medical Students*[*]

College Grade Average First-Year Medical Students		United States									Canada
		1950-1951	1951-1952	1952-1953	1953-1954	1954-1955	1955-1956	1956-1957	1957-1958	1958-1959	1958-1959
3.6-4.0	(A)	40	30	18.0	21.1	16.8	15.8	16.1	17.7	16.0	17.9
2.6-3.5	(B)	43	55	67.5	68.9	69.0	70.6	69.9	66.0	69.7	58.3
1.0-2.5	(C)	17	15	14.5	10.0	14.2	13.6	14.0	16.3	14.3	23.8

[*] Based on returns from 81 medical schools.

that data may be secured for the 1959-1960 academic year regarding the relative importance of the financial factor among the "other reasons" for students leaving medical school despite good academic standing. Although the proportion of these students was relatively large, the actual number (79) was relatively few.

Because the Canadian medical schools do not file class lists and change of status reports of their students with the Liaison Committee on Medical Education, attrition data is not available this year for students in Canadian schools.

TABLE 29.—*Preprofessional Education of First-Year Medical Students in the United States, 1958-1959*

	Size of First-Year Class	Less than Three Years of College	Three Years of College	Four Years of College	Degree	Advanced Degree	% with Degrees
Medical College of Alabama	81	..	15	8	56	2	69.1
University of Arkansas	95	..	42	13	38	2	42.1
College of Medical Evangelists	114	..	..	3	110	1	97.4
University of California, Los Angeles	56	..	5	2	47	2	87.5
University of Southern California	68	..	14	8	42	4	67.6
Stanford University	61	..	17	2	38	4	68.9
University of California, San Francisco	101	..	43	11	45	2	46.5
University of Colorado	86	..	23	15	44	4	55.8
Yale University	81	..	12	2	64	3	82.7
Georgetown University	112	1	4	6	95	6	90.2
George Washington University	101	..	26	6	67	2	68.3
Howard University	105	..	1	2	95	7	97.1
University of Miami	75	..	18	7	46	4	66.7
University of Florida	50	..	4	3	43	..	86.0
Emory University	74	1	20	2	49	2	68.9
Medical College of Georgia	102	..	22	6	71	3	72.5
Chicago Medical School	72	..	..	..	67	5	100.0
Northwestern University	132	..	28	7	90	7	73.5
Stritch School of Medicine of Loyola University	88	..	39	8	41	..	46.6
University of Chicago	73	..	13	7	52	1	72.6
University of Illinois	201	..	106	13	78	4	40.8
Indiana University	160	..	76	24	58	2	37.5
State University of Iowa	120	..	63	13	43	1	36.7
University of Kansas	98	..	..	2	93	3	98.0
University of Louisville	100	..	10	..	88	2	90.0
Louisiana State University	129	..	45	19	61	4	50.4
Tulane University	134	..	66	13	55	..	41.0
Johns Hopkins University	74	..	..	..	70	4	100.0
University of Maryland	100	..	2	7	89	2	91.0
Boston University	74	..	2	3	63	6	93.2
Harvard Medical School	114	..	1	1	111	1	98.2
Tufts University	114	..	1	2	111	..	97.4
University of Michigan	197	..	90	6	95	6	51.3
Wayne State University	125	..	37	16	68	4	57.6
University of Minnesota	139	..	43	21	72	3	54.0
University of Mississippi	78	..	23	20	33	2	44.9
University of Missouri	76	..	17	7	51	1	68.4
St. Louis University	126	..	9	15	101	1	81.0
Washington University	86	..	14	2	70	..	81.4
Creighton University	77	..	27	7	42	1	55.8
University of Nebraska	81	..	33	15	31	2	40.7
Dartmouth Medical School	24	..	22	1	1	..	4.2
Seton Hall College of Medicine	80	..	4	2	74	..	92.5
Albany Medical College of Union University	65	1	4	..	59	1	92.3
University of Buffalo	88	..	8	7	71	2	83.0
Albert Einstein College of Medicine of Yeshiva University	96	..	..	1	93	2	99.0
Columbia University	120	..	..	1	114	5	99.2
Cornell University	86	..	5	2	79	..	91.9
New York Medical College	127	..	1	3	119	4	96.9
New York University	132	..	9	1	117	5	92.4
State University of New York, Downstate Medical Center, New York City	154	..	10	2	136	6	92.2
University of Rochester	69	..	3	..	64	2	95.7
State University of New York, Upstate Medical Center, Syracuse	87	..	7	4	73	3	87.4
University of North Carolina	70	..	12	4	53	1	77.1
Duke University	79	..	10	2	65	2	84.8
Bowman Gray School of Medicine of Wake Forest College	55	..	2	4	49	..	89.1
University of North Dakota	41	..	14	3	24	..	58.5
University of Cincinnati	92	..	3	..	87	2	96.7
Western Reserve University	78	..	4	3	64	7	91.0
Ohio State University	151	..	6	15	123	7	86.1
University of Oklahoma	100	..	38	13	47	2	49.0
University of Oregon	80	..	32	15	32	1	41.3
Hahnemann Medical College	109	..	5	9	89	6	88.0
Jefferson Medical College	175	..	6	2	162	5	95.4
Temple University	136	..	3	5	126	2	94.1
University of Pennsylvania	126	..	..	1	125	..	99.2
Woman's Medical College of Pennsylvania	51	..	1	2	47	1	94.1
University of Pittsburgh	101	..	4	1	94	2	95.0
University of Puerto Rico	55	..	3	8	44	..	80.0
Medical College of South Carolina	80	..	8	2	69	1	87.5
State University of South Dakota	44	..	9	4	29	2	70.5
University of Tennessee	202	..	116	11	70	5	37.1
Meharry Medical College	74	..	6	8	61	4	87.8
Vanderbilt University	52	..	7	6	37	2	75.0
University of Texas Southwestern Medical School	101	..	19	20	59	3	61.4
University of Texas Medical Branch	143	1	33	15	88	6	65.7
Baylor University	84	..	16	5	62	1	75.0
University of Utah	57	..	29	10	18	..	31.6
University of Vermont	51	..	6	..	42	3	88.2
University of Virginia	76	..	7	6	61	2	82.9
Medical College of Virginia	85	..	7	6	71	1	84.7
University of Washington	75	..	26	5	42	2	58.7
West Virginia University	41	..	8	3	27	3	73.2
University of Wisconsin	101	1	57	6	37	..	36.6
Marquette University	105	..	4	6	87	8	90.5
Totals	8,128	5	1,585	513	5,774	221	73.8
					6,538		

GRADUATES

The graduating class awarded the M.D. degree in 1958-1959 numbered 6,860, one fewer than in 1957-1958. These two classes of graduates were the largest except for the 1954-1955 year when the class was 6,977, as table 21 portrays. The bulge in 1954-1955 was occasioned by including as graduates the 50 students completing the intern year then required by Stanford University.

All except 3 of the 79 schools in the United States having graduating classes in 1958-1959 had changes in size of the graduating classes; 43 schools had decreases and 34 schools experienced increases. The range in the former was 1 to 19% down; the range of increase was 1 to 41%.

Three schools had decreases of 15% or more: Arkansas, down 19%; College of Medical Evangelists, down 16%; and Albany, down 15%. An additional five schools experienced decreases of 10% to 15%, as follows: Rochester, down 14%; Nebraska and Texas Medical Branch, each down 13%; and Buffalo and Louisville, each down 10%.

Schools showing increases in size of graduating classes of more than 15% were Mississippi, up 41%; Stritch, up 18%; Meharry, up 17%; and Louisiana State University, up 16%. Five additional schools had increase in number of graduates of 10% or more, as follows: Howard and Oklahoma, each up 12%; and University of Southern California, Yale, and Michigan, each up 10%.

Women comprised 5.4% of the graduating class, as table 34 portrays by school. The two schools having the highest proportion of women graduates, in addition to Woman's Medical College, were the University of Chicago, 13% of class; and University of California, with 12.5% of the class women.

Based on the size of the third-year class in 1958-1959 and the usual attrition in the last two years of school, it is likely that the 1959-1960 graduating class will set a new record high in number, possibly exceeding 7,000. The University of Florida and Seton Hall College of Medicine and Dentistry will have graduating medical classes for the first time in 1959-1960. Albert Einstein College of Medicine had its first graduating class in 1958-1959.

The graduates by sex and school for Canada are also presented in table 34. Half of the 12 Canadian schools had an increase in size of the graduating classes, and the remainder had decreases. The greatest increases were at Ottawa, up 53%; Queen's up 24%; Toronto, up 23%; and Manitoba, up 22%. The largest decreases occurred in Saskatchewan, down 17%; Montreal, down 14%; and Western Ontario, down 11%. The increases in six schools more than offset the fewer graduates in six schools so that the total graduating class was 7 people more than was the case in 1957-1958.

Women comprised 5.9% of the Canadian 1958-1959 graduating class, as compared to 5.2% in the previous year.

STUDENT EXPENSES

In the 58th Annual Report[13] a year ago, estimates of expenses for medical students in the 1959-1960 class were given on the basis of data from the Association of American Medical Colleges. Table 35 presents similar information about students expenses in the 1960-1961 academic year. There appears to be no significant change. As the Association emphasizes in its presentation, the figures given should be regarded as only approximate budgetary goals. They are subject to change in the next year, and there is a considerable range within each of the categories. With tuition and fees, for example, the range is from $592 to $1,400 for private schools, $120 to $786 for residents of that state in publicly owned schools, and $360 to $1,500 for nonresidents in publicly owned schools. Living expenses of individual students vary greatly even in the same school, depending on spending habits and family responsibilities. Tuition in individual schools is included in table 1 for United States schools and table 2 for Canadian schools.

Table 36 presents for the 12 Canadian schools information on student expenses as prepared by the Association of American Medical Colleges comparable to table 35 for the United States. Tuition ranges from $393.25 to $750 for residents. Only three schools cited a nonresident fee and the top one was $859. Tuition is higher in three other schools in the upper years, as detailed in table 2.

TABLE 30.—*Comparative Data About Preprofessional Education of Classes Entering Medical School*

	1936-1937 %	1918-1919 %	1954-1955 %	1955-1956 %	1956-1957 %	1957-1958 %	1958-1959 %
Entering with degree	56.0	55.4	71.1	69.9	72.9	75.6	73.8
	61.0	63.7	74.9	74.8	77.4	79.2	80.4
Entering after four years of college	5.0	8.3	3.8	4.9	4.5	3.6	*6.6
Entering after three years of college	27.0	35.0	21.8	25.1	22.4	20.6	†19.5

* 112 or more semester hours, or 163 or more quarter hours.
† 82-111 semester hours, or 123-163 quarter hours

TABLE 31.—*Comparison of Previous Years and the Current Year of Number and Percentage of Medical Schools Having Entering Classes Consisting Predominantly of Students with College Degrees.*

	1954-1955		1955-1956		1957-1958		1958-1959	
Entering Students with Degrees, %	No. 81	%	No. 85	%	No. 85	%	No. 85	%
100	4	4.9	6	7.0	2	2.3	2	2.3
95.1-99.9	11	13.5	14	16.4	13	15.3	12	14.1
90.1-95	7	8.6	6	7.0	12	14.1	13	15.3
Total	22	27.0	26	30.4	27	31.7	27	31.7

TABLE 32.—*Comparison of Admission Requirements for Medical School Classes Entering in Years 1957-1958 Through 1960-1961*

	Number of Schools			
Stated Admission Requirement	1957-1958	1958-1959	1959-1960	1960-1961
Less than three years college	1*	1*	1*	1*
Three years college	73	74	72	71
Four years college	4	8	10	10
	11	10	12	13
Degree	7	2	2	3
	85	85	85	85

* The same school in each instance, which has actually not admitted any first-year medical students with less than three years of college during at least the past five years.

The reservations expressed regarding the estimates of student expenses in United States schools apply with equal force to estimates of student expenses in the Canadian schools.

MEDICAL STUDENT FINANCIAL PROBLEMS

The Council on Medical Education and Hospitals appreciates the opportunity of presenting in its report the following material prepared at its request by Dr. Leland E. Powers, Associate Director of the Association of American Medical Colleges, who utilized data from an as yet unpublished study by that Association.

The total average expenses, according to family composition, for four years in medical school were tabulated for 4,277 male members of the class. Assuming that expenses were evenly distributed for each of the four years, the average total costs per year would be approximately $2,400 for a single student; $2,800 for a married student; $3,200 for a married student with one child; and $3,900 per year for a married student having two or more children.

TABLE 33.—*Attrition in Medical Schools in the United States (85), 1958-1959*

Year	Enrollment	Withdrawal or Dismissal in Poor Academic Standing	Withdrawal or Dismissal for Other Reasons	Total	Enrollment Lost, %
First ...	8,128	434	253	687	8.4
Second .	7,432	128	89	217	2.9
Third ...	7,182	27	53	80	1.1
Fourth .	6,872	2	26	28	0.4
	29,614	591	421	1,012	3.4

The median age of the 1959 graduating medical student was 26. Sixty-two % of the graduates were married, and of the married students, 48% had one or two children and 7% had three or more children.

A sample study of medical students financial considerations in 1953 by Counts and Stalnaker[14] indicated that about one-third of the medical students expected to be in debt at graduation and 3% expected to be in debt more than $10,000. The preliminary figures for the 1959 graduating class show that 52% are actually in debt, 17% are in debt over $5,000, and 6.5% are in debt more than $10,000.

MARITAL STATUS OF MEDICAL STUDENTS

The annual questionnaire to each medical school this year included, for the first time since 1950, questions about the marital status of medical students. Table 37 presents summary information from the 84 schools providing numerical data, as well as comparative information for the 1949-1950 year as presented in the 50th Annual Report.[15] Since it is generally thought that World War II occasioned an increase in marriage of medical students, it is regrettable that a survey of the marital status of students was not reported during any year prior to 1950.

TABLE 34.—*Medical School Graduates in the United States and Canada by Sex, 1958-1959*

United States	Men	Women	Total
Medical College of Alabama	62	2	64
University of Arkansas	64	5	69
College of Medical Evangelists	78	3	81
University of California, Los Angeles	43	3	46
University of Southern California	63	3	66
Stanford University	54	3	57
University of California, San Francisco	70	10	80
University of Colorado	73	8	81
Yale University	74	5	79
Georgetown University	88	5	93
George Washington University	88	3	91
Howard University	68	7	75
University of Miami	54	5	59
Emory University	64	1	65
Medical College of Georgia	85	3	88
Chicago Medical School	68	..	68
Northwestern University	124	9	133
Stritch School of Medicine	82	4	86
University of Chicago	60	9	69
University of Illinois	148	5	153
Indiana University	136	4	140
State University of Iowa	97	3	100
University of Kansas	97	4	101
University of Louisville	84	2	86
Louisiana State University	108	2	110
Tulane University	114	4	118
Johns Hopkins University	65	3	68
University of Maryland	82	1	83
Boston University	59	7	66
Harvard Medical School	139	8	147
	101	3	104
	179	7	186
	64	2	66
	108	5	113
	61	1	62
	31	..	31
	115	1	116
Washington University	83	5	88
Creighton University	68	2	70
University of Nebraska	69	3	72
Albany Medical College	50	1	51
University of Buffalo	67	3	70
Albert Einstein College of Medicine	47	3	50
Columbia University	109	8	117
Cornell University	76	6	82
New York Medical College	113	10	123
New York University	120	12	132
State University of New York, Downstate Medical Center, New York City	127	11	138
University of Rochester	62	1	63
State University of New York, Upstate Medical Center, Syracuse	61	4	65
University of North Carolina	57	2	59
Duke University	75	3	78
Bowman Gray School of Medicine	45	2	47
University of Cincinnati	75	4	79
Western Reserve University	66	6	72
Ohio State University	135	5	140
University of Oklahoma	87	6	93
University of Oregon	66	..	66
Hahnemann Medical College	89	4	93
Jefferson Medical College	166	..	166
Temple University	109	6	115
University of Pennsylvania	123	2	125
Woman's Medical College of Pennsylvania	...	41	41
University of Pittsburgh	78	2	80
University of Puerto Rico	38	5	43
Medical College of South Carolina	70	4	74
University of Tennessee	163	10	173
Meharry Medical College	61	6	67
Vanderbilt University	47	1	48
University of Texas, Southwestern	84	7	91
University of Texas, Medical Branch	125	7	132
Baylor University	69	4	73
University of Utah	48	..	48
University of Vermont	36	4	40
University of Virginia	64	4	68
Medical College of Virginia	88	6	94
University of Washington	65	3	68
University of Wisconsin	68	3	71
Marquette University	91	4	95
Totals	6,490	370	6,860
Canada			
University of Alberta	49	1	50
University of British Columbia	40	4	44
University of Manitoba	52	3	55
Dalhousie University	49	3	52
Queen's University	54	2	56
University of Ottawa	53	2	55
University of Western Ontario	46	5	51
University of Toronto	138	9	147
McGill University	92	6	98
University of Montreal	91	6	97
Laval University	118	6	124
University of Saskatchewan	26	4	30
Totals	808	51	859

It appears that there is little significant change in the total proportions of married students by class since the 1949-1950 year with the exception of a 5% diminution in fourth-year married students in 1958-1959 as compared to nine years previously.

TABLE 35.—*Estimates of Median Minimum Expenses for First-Year Medical Students in United States**

Item	Private Schools (N-45)	Public Schools (N-44) Resident	Public Schools (N-44) Nonresident
Tuition and fees	$1,050	$498	$830†
Room and board	800	700	700
Books and supplies (not including microscopes)	150	125	125

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* Reprinted from "Admission Requirements of American Medical Colleges (including Canada), 1959-1960", for applicants to the 1960-1961 class, published by the Association of American Medical Colleges, Evanston, Ill., including newly forming University of Kentucky School of Medicine, Lexington because it will accept students for classes beginning September, 1960.

† Excluding two schools that accept no nonresidents in the first-year class and two schools that accept no nonresidents at all. Two private schools cite higher tuition for nonresidents

About one-fourth of students in the first or entering class are married. This increases to more than one-half of the fourth-year students being married. The ranges are wide among students bodies in the various schools, as shown in table 37.

Table 38 compares the first-year and fourth-year classes as to proportions of students married. It clearly portrays the increasing proportions of married students by the fourth year. Whereas no school reported having more than 75% of first-year students married, 10 schools reported that high a proportion of fourth-year students married. For fourth-year students, only two schools (Woman's and Puerto Rico) could report less than 30% of the class as married, and 61 schools in all reported more than one-half of the senior class as married. Of the total of 11,945 married students, 200 are known to be married to other medical students.

Study of table 38 reveals an interesting difference in the marital status of students in publicly owned as compared to those in privately owned schools, both for first-year and fourth-year students.

TABLE 36.—*Estimates of Median Minimum Expenses for First-Year Medical Students (Canadian Dollars)**

First-year-Expense Item	Median Amount Cited by Medical Schools of Canada
Tuition and fees (resident)	$515.00
Room and board (minimum)	612.50
Books and supplies (not including microscopes)	105.00

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* Reprinted from "Admission Requirements of American Medical Colleges (including Canada), 1959-1960," for applicants to the 1960-1961 class, published by Association of American Medical Colleges, Evanston, Ill.

Higher proportions of students in publicly owned schools are married than is the case in the privately owned medical schools. Of 4,035 first year students enrolled in 44 privately owned medical schools, 866 or 21.5% are married, as compared to 1,275 or 32.2% of the 3,961 first year students married in the 45 publicly owned schools. For fourth-year students, of 3,566 enrolled in 44 privately owned schools, 1,836 or 51.5% are married, while 1,953 or 61.5% of 3,175 students are married in the publicly owned medical schools. As table 38 shows, though 37 of the 44 privately owned schools which reported on marital status had first year classes in which less than 31% of the students were married, only 19 of the 40 publicly owned schools had first year classes with that small a proportion of married students. On the basis of available information, one may only speculate on the causes of this difference.

TABLE 37.—*Marital Status of Medical Students*

Year	Total Enrollment	Number Married	% Married 1958-1959	Range in % of Classes	% Married 1949-1950*
		U.S.A.			
First	7,996†	2,141	26.8	1.8-56.1	24.7
Second	7,302†	2,662	36.5	5.7-72.7	35.6
Third	7,049†	3,353	47.6	9.7-73.9	46.9
Fourth	6,741†	3,789	56.2	17.1-83.3	61.2
		Canada			
First	772‡	60	7.8	1.4-20	
Second	703‡	[illegible]	11.5	2.3-30	
Third	673‡	126	18.7	7.3-31.4	
Fourth	701‡	219	31.1	14.2-53.7	

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† Corrected by deleting enrollments in one school not reporting on marital status.

* From 50th Annual Report on Medical Education in U. S. and Canada, J. A. M. A. 144:118-119 (Sept. 9) 1950.

‡ Corrected by deleting enrollments in two Canadian schools not reporting on marital status.

Of the 12 Canadian medical schools, 10 supplied information about the number of married students. In each medical year, a materially smaller proportion of students in Canadian schools than in United States schools are married. Table 37 presents the information in summary form about the students in Canadian medical schools. Fewer than one-tenth of first-year students are married and by the fourth year, less than one-third of the students have married. The ranges in the 10 Canadian schools are also less wide than in the case in the United States medical schools. For first-year students, one school reported 30% of the class married, and four additional schools reported 20% or more of the class as married. Only two Canadian schools reported 50% or more of fourth-year classes married, and three additional schools reported 40% or more of fourth-year students married. By the time they had reached their fourth year, married students in only two schools

TABLE 38.—*Comparison of Proportions of Classes Married,* First and Fourth Years, 1958-1959*

15% or less married	16-30%	31-50%	51-75%	over 75%
		First-Year Students		
12 schools	44 schools	25 schools	3 schools	None
10 Privately owned	27 Privately owned	5 Privately owned	2 Privately owned	
2 Publicly owned	17 Publicly owned	20 Publicly owned	1 Publicly owned	
		Fourth-Year Students		
None	2 schools	21 schools	51 schools	10 schools
	1 Privately owned	17 Privately owned	23 Privately owned	3 Privately owned
	1 Publicly owned	4 Publicly owned	28 Publicly owned	7 Publicly owned

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* Corrected by deleting one school not reporting on marital status.

comprised less than 20% of the class. Of the 507 married students, only 12 were known to married to other medical students.

STUDENT HOUSING

Information regarding student housing under medical school control was requested from the medical schools this year. In response, it appears that 45 of the 85 schools in the United States have no such apartments or dormitories for medical students. Of the 40 responding in some degree affirmatively, 38 definitely have some housing under medical school (32) or university (6) control, and 2 replies stated "housing facilities available" without clearly indicating the nature of the control.

Five schools can accommodate 100% of the total medical student body in such apartments or dormitories (Arkansas, Yale, Minnesota, Missouri, and Cornell). Five other schools have 82 to 96% of their medical student classes in university or medical school housing (Indiana, Iowa, Johns Hopkins, Columbia, and South Carolina). Eight schools provided housing for 3.1 to 15.2% of their medical students, 9 schools provided for 16.2 to 29.9%, 8 schools for 31 to 46.2% of their students, and 5 schools provided housing for 52 to 71.5% of their medical students.

Of the schools providing housing, the median proportion of the student body accommodated in 1958-1959 was 36% and the average was 45%. The range was 3.1 to 100%. Three schools reported more students housed than they reported as total medical students, indicating that other students than medical students were reported occupying university or medical school controlled housing. In computing the average, these three were considered as 100%.

Eighteen of the 40 schools providing housing in 1958-1959 had single men, single women, and married students in the units. Seven schools had only single men so housed, eight schools had only single men and single women in their housing, one school had only married students in medical school controlled living units, and the remainder had various other combinations of single and married students.

Of the schools reporting medical students housed in medical school or university controlled housing, 29 schools reported without special qualification the yearly rental per student per year for men, 22 schools for rental to women, and 16 schools rental to married students. The average minimum rental per man per year was $322.11, and the median was $269. For women, the minimum average of the 22 schools was $387.84 and the median was $324.50. For married students with 16 schools reporting without incomparable qualification, the minimum average yearly rental was $633.48; the median was $653.75. The average and median rental figures for married students should engender some reservation; however, inasmuch as it is possible that some of the schools may have reported rentals per couple rather than per student. However, the rental ranges were great, as follows: for single men, $140 to $840 a year; for single women, $140 to $900; and for married students, $171 to $1,050 per student.

REPORTS OF CURRENT INTEREST TO MEDICAL EDUCATION

SECOND WORLD CONFERENCE ON MEDICAL EDUCATION

The Second World Conference on Medical Education in Chicago, Aug. 30-Sept. 4, 1959, attracted 610 registrants from 66 countries to hear 48 participants from throughout the world. The Conference was sponsored by the World Medical Association in collaboration with the World Health Organization, the Council for International Organizations of Medical Sciences, and the International Association of Universities, assisted by the American Medical Association and the Association of American Medical Colleges. Its theme was medicine—a lifelong study.

Dr. Raymond B. Allen was president of the Conference, Dr. Ray F. Farquharson of Canada and Dr. Victor Johnson were deputy presidents. Rapporteurs were Dr. F. Hugh Luckey, Dr. Thomas B. Turner, Dr. Oliver Cope, and Dr. Stanley S. B. Gilder, Canada.

In all sessions there was simultaneous translation of the discussions into French, Spanish, and English.

Viewpoints were exchanged regarding the activities and challenges in various countries about the four major subject areas of the Conference: (1) basic clinical training for all doctors, (2) advancing training for general and specialty practice, (3) the development of teachers and investigators, and (4) continuing medical education. An initial plenary session was followed by simultaneous sessions on these subjects during two half days, and one whole day with a summary plenary session. Included also in the overall program were technical and scientific exhibits of interest to the international assembly of medical educators, as well as opportunities to visit medical institutions in Chicago or review medical motion pictures and television programs.

The papers presented and the discussion will be published as proceedings in book form by the World Medical Association, 10 Columbus Circle, New York City 19. Papers presented to the initial plenary session August 31 were published in THE JOURNAL.[17]

The American Medical Education Foundation

On Feb. 9, 1959, the American Medical Education Foundation made grants from the 1958 income of $1,133,258 to the eighty-five medical schools in the United States. Of these contributions, $627,958 were in the form of earmarked gifts from physicians to specified schools. The balance was distributed equally. This brought the total that the Foundation has raised and distributed from the medical profession to $7,874,723 since 1951.

The American Medical Education Foundation, sponsored by the American Medical Association, which pays all of the cost of AMEF's administration and promotion, has developed a deep interest for the financial problems of medical education in most of the state and county societies across the country. A corollary interest in the educational problems of these schools has also been developed while presenting the schools' monetary needs.

The activities of the Foundation, in its effort to stimulate giving, have been brought to the attention of the entire profession. Editorials have been printed in every medical journal in the United States. Advertisements have been run in a great number of these journals. Exhibits have been displayed at many state and national medical meetings. The officers and the staff of the Foundation have spoken in general meetings and to the Houses of Delegates of a large majority of the societies. The state chairmen and committeemen have presented the urgent needs of the schools to county meetings and in reports to state societies.

The national office has sent two or three mailings a year to the entire profession and distributed brochures and promotional material to the state societies, who, in turn, have made many mailings themselves. With the help of the Foundation staff and the executive staffs of the state associations, highly organized solicitation campaigns have been conducted in many states. Six states now have a compulsory item on their dues bill for the American Medical Education Foundation. Six others include this as a voluntary item on their dues statement. Surprisingly, the physicians in these states that use the dues statement method are at least as enthusiastic about the program as those that go to the great efforts of voluntary campaigning.

During the past three years the Foundation has also worked out coordinated programs of various natures with several of the medical schools themselves. Particularly successful in this has been the Georgetown-AMEF joint appeal.

On many of the state campaign committees, and on some of the local campaign committees, representatives from the medical schools, such as deans, assistant deans, or faculty members have been asked to serve. This has resulted in greater cooperation and understanding between the societies and the schools. One outstanding example of this has been in a city in the south where some misunderstandings were resolved in the joint efforts put forth by all for the AMEF program.

The Foundation has also assisted the schools by collecting and tabulating the results of the appeals to physicians from the schools themselves. Last year $3,034,406 in contributions from 55,246 physicians were recorded in the Foundation office. An important policy of the Foundation—the emphasis on unrestricted gifts—has been adopted as a responsibility which the Foundation has continued to publicize.

It is hoped that the Foundation's continued insistence on unrestricted gifts will assist the schools in securing similar releases from other sources of support.

The Foundation's grants are made without stipulation, or rather, it is stipulated that they are to be used as the dean and the medical school administration feel they are most needed. In addition, it is emphasized that the grants are extra budgetary in nature and are to be considered as support for programs where no other moneys are available, or as an increment to inadequate appropriations from basic sources.

NATIONAL FUND FOR MEDICAL EDUCATION

The accompanying résumé has been submitted by the staff of the National Fund for Medical Education to acquaint readers with the current activities of the Fund in support of medical education.

The National Fund for Medical Education in March, 1959, awarded grants totaling $2,925,180 to the nation's 82 accredited medical schools. This brought to $18,743,946 the total distributed by the Fund since its first grants were made in 1951.

Each four-year school received $15,000 plus $60 per undergraduate medical student. The four two-year medical schools of the basic medical sciences received $7,500 each, plus $60 per student.

In addition, in May, the Fund made grants totaling $75,000 to 11 medical schools, under its special Class C Grants Program, to help American educators find ways to cope with teaching problems growing out of the rapid advancement of the medical sciences. These grants ranged in size from $360 to $14,000 and were given on a one-year basis.

The Fund's grants were made possible through the generosity of some 1,946 corporations, which contributed $2,046,399, as well as through a Ford Foundation grant of $1,027,705, under its "matching" arrangement with the Fund.

In July, 1958, the Fund established its Medical Research Program through which contributions from united funds, community chests, voluntary health agencies, and other programs would be channeled into basic medical research. The program will aim to help support the continuing search for new medical knowledge and to increase the number of trained medical researchers in the U. S. by stimulating interest in basic research. Many local community chests and united funds are supporting the Medical Research Program.

This expansion of the Fund's program will in no way affect its present campaign among corporations to obtain support for the teaching budgets of the medical schools. The first grants under the Medical Research Program will be made in the winter of 1960 to the 85 medical schools.

In September, 1959, the Fund joined with the American Medical Association and the Association of American Medical Colleges in presenting the seventh Frank H. Lahey Memorial Award to Devereux C. Josephs, former Chairman of the Board, New York Life Insurance Company, and Chairman of the Fund's Grants Review Board. This award is given annually to a layman for "distinguished service to medical education." Previous recipients have been President Dwight D. Eisenhower, former President Herbert Hoover, Dr. Abraham Flexner, Colby M. Chester, Alfred P. Sloan Jr., and Frank Abrams.

The Fund is continuing its campaign to alert American corporations to the problems and needs of medical education. Over the years its experience has demonstrated that American management is increasingly recognizing its responsibility to help create a healthy, strong and resourceful nation. Corporation directors, the Fund feels certain, are becoming more and more aware that medical education is a focal point of national strength and they are ready, we believe, and willing to take their place in the ranks of those supporting medical education if the facts can be brought to their attention in the proper fashion. That has been the Fund's job and will continue to be its job in 1960.

NATIONAL INSTITUTES OF HEALTH STUDY OF TWENTY MEDICAL SCHOOLS

On November 1, 1958, Dr. James A. Shannon, Director of the National Institutes of Health, appointed a Staff Committee on Support for Medical Research and Training to evaluate the impact of research growth on medical schools and to make recommendations for measures that NIH might undertake "to facilitate the present conduct and further development of medical research at schools of medicine." The Committee, chaired by Dr. Kenneth M. Endicott, Associate Director, NIH, reported in April, 1959, after a three month full time period of collecting and analyzing the data. Questionnaires and visits to the 11 publicly owned and 9 privately owned schools provided the data.

Comparative data for 1948 were obtained from the Surgeon General's Committee on Medical School Grants and Finances, 1949. The schools projected estimates for 1970.

It is believed that the 20 schools selected were, as nearly as possible, a representative group.

The study outline covered the following areas:

1. Developments over the past decade: (*a*) changes in the school's sources of income and pattern of expenditure; (*b*) changes in faculty and staff; (*c*) changes in enrollment levels; and (*d*) construction of new facilities.

2. An appraisal of current NIH mechanisms for support of research and training, their strengths and weaknesses, and discussion of whether changes in policy and procedure should be considered.

3. A consideration of medical school views regarding the major recommendations of the Bayne-Jones report.

4. A projection of future developments at each school on the assumption that financial support would increase.

General trends shown were that during the past decade, schools have grown rapidly in response to demands. Full-time faculty have doubled, expenditures have tripled, and $130,000,000 was spent on construction. By 1970, if funds are available, these trends will continue. Full-time faculty personnel will increase by almost two-thirds, expenditures will double, and $420,000,000 will be spent on construction. It was reported that most of the growth has been related to increased emphasis on research, to the increasing complexity of medical education, and to the schools' expanding role in the training of personnel for research, for clinical specialties, and for professions allied to medicine.

As to medical student graduating classes, it was estimated that these might be increased by one-third if additional two-year schools of basic medical sciences were created, but that the present schools could accommodate no more than a 21% increase in entering medical students. The 20 schools in the study need and will continue to need third year medical student transfers of about 10% the size of their entering classes. If all 85 schools increased their first year enrollment by 21% during the next decade, based on the current entering class of 8,128, 9,636 students could be admitted. If increased funds permitted both an increase in size of entering classes as estimated, and two-year schools added 788 students to third year classes in the 81 schools, then 9,148 total students could be graduated. It is estimated that in five years there would be an expansion also of 50% in medical student research trainees, 49% in graduate and postdoctoral nonclinical programs, 21% in students in allied or paramedical areas, 86% in clinical fellows and trainees, and 34% in students in other clinical education including continuation courses.

The importance of federal research and training grants in medical school expenditures was evident. In 1948, such federal support comprised 9% of total budgets. This increased to 29% in 1958 and it was estimated it will be 44% of total medical school expenditures by 1970. The surveyed schools had received about $25,000,000 in federal construction grants and estimated the need for more than $130,000,000 in federal construction grants for the period 1958-1970.

The study revealed that separately budgeted research in 1958 comprised 42% of medical school budgets as compared to 22% in 1948. The Committee's estimate of the total cost of research in nine public and seven private medical schools studied was $34,100,000, of which the gifts, grants and contracts provided only $23,900,000, with $10,200,000 coming from the medical school institutional funds. Thus, because the gifts and grants seldom paid the full cost of the particular project for which they were awarded and because such funds made up an increasingly large segment of medical school expenditures, one result was that the schools had proportionately less and less fluid money. The schools studied emphasized their need for fluid funds.

Another impact of the research and training grants was on faculties. There is an increasing proportion of non-tenure faculty members supported by grants who are denied permanent appointments because the schools have not in sight requisite state appropriations or endowment income. Lack of permanent faculty appointments denies the grant-supported personnel a number of tangible and intangible benefits. If research is to attract and hold outstanding people, the Committee stated that this situation must be overcome. The study noted that 36% of the paid, full-time faculty of the schools studied received all or part of their salaries from gifts, grants, and contracts.

The Staff Committee recommended that the Public Health Service, an agency which is intimately involved and deeply concerned and in a position to provide leadership to rally support for the schools from other groups, take the following steps:

1. Modify and expand existing programs that aid in construction of medical school facilities;
2. Establish a new program of institutional research grants to improve and stabilize the rapidly growing research programs by providing fluid funds that schools will feel justified in using to underwrite permanent appointments for research staff;
3. Provide for payment of the full costs of research;
4. Extend the senior research fellowship program to meet urgent needs in clinical as well as in preclinical areas;
5. Expand research grant and training programs.

In addition, the Staff Committee recommended for less immediate implementation, a study of the needs of medical schools for general operating funds and the needs of medical students for some form of financial assistance, as well as consideration of the possible value of initiating a series of national conferences on medical research and medical education.[9]

THE SURGEON GENERAL'S CONSULTANT GROUP ON MEDICAL EDUCATION

Late in 1958, the Surgeon General of the Public Health Service established a Consultant Group on Medical Education. The group of more than twenty prominent and knowledgeable individuals were requested to consider the question: "How shall the nation be supplied with adequate numbers of well-qualified physicians?" The study with accompanying recommendations is expected to be published shortly. The findings of this deliberative body should prove to be of great value to those individuals and organizations interested in and concerned with future medical manpower needs.

INTERNATIONAL EDUCATIONAL EXCHANGE IN MEDICINE

The annual issue of "Open Doors,"[10] published in May, 1959, by the Institute of International Education presents a valuable and detailed report on the international exchange of students, faculty members, and physicians between the United States and other countries. The Institute annually conducts five surveys which form the basis for its yearly report. According to the Institute's current surveys, there are more foreign citizens in the United States for educational purposes than ever before. The following is quoted from the introductory paragraphs of the 1959 report.

> There were 57,574 foreign citizens on educational assignment in the United States during the academic year 1958-1959. This represents a 10% increase over 1957-1958, when 52,355 foreign citizens were reported. 47,245 of this year's foreign citizens were students; 1,937 were foreign lecturers, professors or researchers who had received appointments to American faculties and 8,392 were foreign interns and residents affiliated with hospitals in the United States.
>
> The foreign nationals included in Open Doors are citizens of other countries who have come to the United States for educational purposes and who intend to return home upon the completion of their assignment. Displaced persons who are settling in the United States and foreign citizens who are establishing permanent residence in the United States are not included.
>
> These visitors represent every major geographical and political area. As in previous years, the largest number of exchangees came from the Far East and the second largest number from Latin America. The 19,431 nationals from Far Eastern countries were 33.7% of the entire foreign population, and the 12,111 from Latin America represented 21%.
>
> 9,025 students, physicians and faculty members came from Europe; 8,082 from the Near and Middle East, and 6,177 from North America (Bermuda and Canada). Even though more citizens of the countries of Africa and Oceania are in the United States this year than last, they still constitute a small proportion of the exchangees.
>
> The total number of U. S. citizens reported—faculty members for 1958-1959 and students in 1957-1958—showed a 17% decrease from last year's published figure of 14,534 U. S. citizens abroad for educational purposes. The majority of American scholars went, as in previous years, to Europe. Fewer Americans were reported in Latin America, Canada and the Far East, but in spite of the over-all decrease there was an increase in the number of Americans in the Near and Middle East and Oceania.

Of particular interest are the approximately 645 foreign students enrolled in premedical studies, 1,154 in medicine (undergraduate and graduate but excluding internship and residency) and 1,742 enrolled as undergraduate or graduate students in the general field of biological sciences.

Visiting Foreign Scholars on Faculties of United States Educational Institutions

The Institute reported that during the 1958-1959 academic year there were, for the first time since its surveys were initiated, more foreign professors, instructors, lecturers, and advanced research scholars on the faculties of United States colleges and universities than there were United States faculty members abroad. There were 1,937 foreign faculty members reported on United States faculties and only 1,842 United States faculty members reported abroad. Last year there were 1,342 visiting foreign scholars at 222 United States colleges and universities. This year, 288 institutions welcomed 1,937 faculty members to their campuses. The scholars in the United States represented 71 countries.

Table 39.—*Foreign Students in Medical Schools in the United States, 1958-1959*

Area	Countries, No.	Students, No.
Far East	12	93
Near and Middle East	9	53
Europe	12	70
Latin America		
Caribbean	9	58
Central America	6	20
South America	8	28
Africa	7	22
Oceania	2	2
Total	65	346

The largest group of visiting foreign faculty members, 907, were in the natural and physical sciences; 286 scholars served on medical faculties; 270 in the various fields of the humanities; 179 in the social sciences; 177 in engineering; 44 in agriculture; 42 in education; and 32 in business administration.

Foreign Students Studying Medicine in the United States and Canada, 1958-1959

In 1958-1959, there were a total of 346 foreign students enrolled in United States medical schools (table 39). These students represented 65 different countries and are studying medicine in 63 of the 85 United States schools. Included in this total of 346 are 110 foreign students who were admitted to the entering class of 47 schools. In addition, 86 students were enrolled in the second year, 80 in the third year, and 70 in the fourth year. Table 40 gives, for five academic sessions, the number of students from foreign countries admitted to medical schools in the United States as entering students to the first year class.

Table 40.—*Foreign Citizens Enrolled in Entering Class of Medical Schools of United States, 1954-1959*

School Year	No. Foreign Students in Entering Class
1954-1955	94
1955-1956	97
1956-1957	92
1957-1958	73
1958-1959	110

The 12 medical schools in Canada enrolled 86 foreign students from 21 countries and 219 citizens of the United States, a total of 305 students. The areas represented and the number of students from each area are included in table 41.

Table 41.—*Foreign Students in Medical Schools in Canada, 1958-1959*

Area	Countries, No.	Students, No.
Far East	4	35
Near and Middle East	3	3
Europe	6	12
Latin America		
Caribbean	2	3
Central America	2	2
South America	1	1
Africa	3	9
United States	..	219
Other*	..	21
Total	21	305

* Countries not specified

United States Citizens Studying Medicine Abroad

The Institute of International Education presents in its "Open Doors" the total number of the United States students studying but does not break the figure down into major fields of study. There appears to be no accurate calculation available of the number of students studying medicine abroad. It appears likely, however, when compared to the ratio of applicants to admissions in United States schools, that many of the American students now studying medicine abroad were not considered qualified for such study in United States schools.

It has been possible for the past several years to collect data pertaining to the numbers of American-born graduates of medical schools outside of the United States and Canada who have received their initial medical licenses in the United States. Table 42 records accumulated figures from 1950-1954 and yearly data for succeeding years. Such data were not available for New York, which licenses a good proportion of foreign physicians and Pennsylvania with a more normal complement prior to 1956. Beginning in 1956 when returns were available from all states, it will be noted that the figure is steadily increasing, showing an increase

Table 42.—*Initial United States Licenses Issued to American Graduates of Foreign (Excluding Canada) Medical Schools*

Year	No. of Licenses Issued	No. of States
1950-1954	90	20
1955	89	19
1956	103	15
1957	212	17
1958	284	26

of 72 in 1958 over the previous year. It can be predicted that this figure will increase as the students abroad complete their training and return to the United States.

Foreign Physicians Training in United States Hospitals

In terms of numbers of students involved, the greatest contribution by American medicine to the medical education of foreign physicians continues to be at the graduate level. The Institute of International Education's survey of foreign physicians training in United States hospitals, as reported in "Open Doors," is as follows:

> During the 1958-1959 academic year, 8,392 physicians from 91 countries trained in United States hospitals. 6,068 trained as resident physicians and 2,324 as interns. These figures represent an increase of 770 physicians over the 7,622 reported last year. 3,109 physicians were in the United States from the Far East, 1,737 from Latin America, 1,331 from the Near and Middle East and 1,480 from Europe.
>
> Most foreign areas showed an increase in the number of physicians reported. The number of physicians from the Near and Middle East increased approximately 25%. An increase of 19% was reported from the Far East; 493 more physicians were in the United States from this area. Of this the Philippines alone accounted for an increase of 384 men and women in medicine. The number of physicians from Europe decreased. 153 or 9% fewer doctors from European countries were reported at United States hospitals this year. [Table 43.]
>
> Foreign physicians trained in 40 states, the District of Columbia, Hawaii, and Puerto Rico. 27% of all foreign physicians were located in New York. There is such a wide distribution of foreign physicians throughout the United States that only 10 institutions reported more than 50 foreign physicians. These 10 hospitals only accommodate slightly more than 7% of the total number of foreign physicians. [Table 44.]

United States Faculty Members Abroad

During the 1958-1959 academic year, 1,842 faculty members from 367 United States colleges and universities were on teaching or research assignments in 82 foreign countries. Of these, 124 were members of medical faculties. On this aspect of its studies, the Institute of International Education points out that the United Kingdom received the largest percentage of American scholars, 17% of all faculty members abroad were in the United Kingdom. France was second with 132, or 7%, of the American scholars. As in previous years, the humanities, the social sciences, and the natural and physical sciences are the leading fields. Education, medicine, agriculture, engineering, and business administration follow in that order. The number of scholars in the natural and physical sciences and in medicine showed a sharp increase, while the fields of education, agriculture, and engineering showed a sharp decrease. There were 389 scholars reported in the natural and physical sciences as compared to 272 last year. Medical faculty members increased from 107 to 124.

TABLE 43.—*Leading Nationality Groups of Foreign Physicians in the United States*

Nationality Group	No. of Physicians
Philippine Islands	1,982
Turkey	650
Canada	563
Mexico	512
Iran	402
Korea	304
Greece	296
Japan	287
India	279
Germany	269

TABLE 44.—*Ten Hospitals with More than Fifty Foreign Physicians*

Hospital	No.
Bellevue Hospital Center, New York	91
Memorial Center for Cancer and Allied Diseases, New York	80
Cumberland Hospital, Brooklyn, New York	68
Kings County Medical Center, Brooklyn, New York	67
Elmhurst General Hospital, Elmhurst, New York	66
Jersey City Medical Center, Jersey City, N. J.	56
Henry Ford Hospital, Detroit, Michigan	55
Lincoln Hospital, New York	54
Cuyahoga County Hospital, Cleveland, Ohio	51
Peter Bent Brigham Hospital, Boston, Mass.	51

AREAS ALLIED TO MEDICINE

SCHOOLS FOR MEDICAL RECORD LIBRARIANS

The Council has worked closely with the American Association of Medical Record Librarians since 1942 in the development of criteria for and evaluation of educational programs in medical record library science. Initial and continued approvals of schools are considered by the Council on the basis of the recommendations of the Education and Registration Committee of the American Association of Medical Record Librarians, which has an able education director who makes periodic survey-visits to schools.

Significant studies to further advance training in the field have been carried out by the American Association of Medical Record Librarians.

Revision of the curriculum currently recommended by the Council and the American Association of Medical Record Librarians is under active consideration. Revisions which are expected to be adopted in 1959-1960 will be gradually implemented over a period of several years.

As of June 30, 1959, there were 30 approved schools. Student enrollment increased in 1958 to 169 students in the senior class of degree programs and in certificate programs, which represents a 1% increase over 1957. There was a training capacity for 246 students in these programs. Accordingly, the occupancy rate was 42% for the senior class of 9 degree programs with senior students in 1958 and 83% in the 21 active certificate programs. Since no students were enrolled in one school offering only a degree program but students were separately enrolled in both programs offered by one school, students were enrolled in 30 programs offered by 29 schools. The number of graduates in 1958 for 10 degree programs was 18. In addition, there were 79 graduates from 21 certificate programs or a total of 97 graduates from 26 schools in 1958. In 1957, 26 degree and certificate programs graduated 139 medical record librarians. Since June 1959, three educational programs have been discontinued and two have been inactivated for the academic years 1959-1961. Approvals for two new university programs in medical record science are pending.

Approved schools offer curricula which include theoretical instruction and practical training in hospitals. When the hospital training is sequentially and properly integrated with collegiate studies, a degree is available after four years of study. As of June 30, 1958, among the 10 schools offering degree programs, 7 admit qualified high school graduates, and 3 schools require three years of preparatory college. In the 21 schools offering certificate programs of one year's duration, 17 require two years of college prior to admission. All but 3 of these 17 schools will also admit graduates from an accredited school of professional nursing of at least three years' duration. A college degree is required for admission into 4 certificate programs. Lists of approved schools are available from the Council. Applicants should write directly to the Medical Record Librarian-Director of the School.

Schools conducting degree programs usually begin in June, and the majority of certificate programs admit students in September. Tuition ranges from $125 to several hundreds of dollars per year and 2 schools require none. A hospital or university should apply to the Council on Medical Education and Hospitals of the American Medical Association for approval.

SCHOOLS FOR MEDICAL RECORD TECHNICIANS

Schools for medical record technicians are conducted to train the medical record technician who, working under the supervision of a qualified medical record librarian or a medical record committee, performs the technical tasks associated with the maintenance and custody of medical records.

As in the case of medical record librarians, the Council has developed educational criteria for and evaluates schools in close collaboration with the American Association of Medical Record Librarians.

The training of medical record technicians should be conducted in acceptable general hospitals having a minimum of 4,000 admissions. These admissions should include an adequate distribution of patients in the various clinical services commonly found in general hospitals. Candidates for admission to an approved school should be proficient in typing and preferably also in shorthand. They should have completed the requirements for high school graduation or should have passed a college entrance examination for admission to an accredited college or university. The minimum length of training is nine months and should include theoretical instruction in anatomy, medical terminology and medical records, with additional practical training in admitting and discharge procedures, indexing, preparation of reports, and other activities associated with the medical record department.

There are 12 hospitals approved by the Council for training medical record technicians. These schools reported a training capacity for 78 students with an enrollment of 55 students and 40 graduates in 1958. Data for 1957 are 11 schools with a training capacity for 73 students, an enrollment of 58 and 37 graduates. Qualified high school graduates are accepted for courses of from 9-12 months duration.

Hospitals should apply to the Council on Medical Education and Hospitals for approval. Special forms will be supplied for this purpose, and, when the required information has been received, the proposed training program will be reviewed in collaboration with the Committee on Education and Registration of the American Association of Medical Record Librarians. The institutions applying for Council approval will, in all instances, receive full information and every possible assistance in the planning and development of training programs in accordance with present standards. There continues to be an acute shortage of qualified medical record librarians and medical record technicians. Excellent opportunities exist for graduating students. Inquiries on career opportunities, registration, and accreditation of qualified medical record personnel should be addressed to the American Association of Medical Record Librarians, 840 North Lake Shore Drive, Chicago 11.

SCHOOLS FOR MEDICAL TECHNOLOGISTS

In its continuing efforts to assist hospitals in the development of training programs for medical technologists, the Council cooperates closely with the American Society of Clinical Pathologists, the Board of Schools of Medical Technology, the Board of Registry of the Society, and the American Society of Medical Technologists. The Board of Schools was established by the society in 1949 to serve as the major advisory body to the Council in all matters relating to standards and the evaluation of educational programs. Revisions of the standards occurred in 1941, 1943, 1947, 1949, 1953, and June, 1958. The significant revision is that, effective Jan. 1, 1962, entrance requirements will be increased from two to three years of pretechnical collegiate education. No major change has been made in the 12 months' technical curriculum in the hospital. It is expected that the third year of college will provide emphasis on general education yet also afford, in appropriate balance, selected courses to broaden the students' science background. Schools not currently affiliated with colleges and universities are encouraged to consider affiliation or affiliations whereby a consecutive educational sequence of three years of college and one year of hospital training will lead to a baccalaureate degree. While such affiliation is not required, it is encouraged on the basis of the inherent educational benefits to students and faculties and the favorable experience of currently affiliated hospital schools.

As of June 30, 1959, there were 702 approved schools, or an increase of 3% over the 681 schools approved in 1958. Enrollment increased 4% to 3,209 students in 1958 and the number of graduates was 2,345, which represents a 3% increase over 1957. With a student capacity of 5,345 the occupancy rate in 1958 was 60%.

Seventy-seven per cent, or 538 training programs, base admission on two years of college; 130 (18%) require three years of preclinical college education; and 34, or 5%, require a baccalaureate degree for admission.

The number of hospital schools with college or university affiliations continues to increase. In 1958, a total of 503 hospital schools (72%) had college or university affiliations. Such affiliations as noted above are strongly encouraged since they stimulate the development of well-organized training programs suitably integrated with the college curriculum and also serve as a continuing source of students. If properly integrated, a degree is available upon completion of three years of college education followed by one year of hospital training in 474 (68%) of the 702 approved schools. Active liaison between the hospital and the affiliated college is strongly recommended through regularly scheduled meetings of an advisory or coordinating committee comprised of representatives from each faculty.

The minimum duration of the hospital course acceptable for approval is 12 months. Ninety-one per cent, or 636 schools, offer a course of 12 months' duration. The remaining 9% of the programs vary from 12½ to 36 months in length. Tuition is required by 139 (20%) and a minimal breakage fee by 77, or less than 11%, of the schools. Students receive a stipend in 400 (57%). All states except Alaska, the District of Columbia, the Canal Zone, and Puerto Rico have approved schools. Interested high school students should apply to accredited colleges and universities of their choice; those students in college or with collegiate backgrounds should apply to the pathologist-director of the laboratory school of their choice. Lists of approved schools of medical technology, which indicate those schools that have college affiliations, are available from the Council.

Application for approval of a school for the training of medical technologists should be made to the Council on Medical Education and Hospitals of the American Medical Association. Forms will be supplied for this purpose on request and should be completed by the director of the laboratory requesting this approval. Inquiries regarding the registration of qualified medical technologists should be addressed to the Board of Registry of Medical Technologists, P. O. Box 44, Muncie, Indiana.

SCHOOLS FOR OCCUPATIONAL THERAPISTS

Through a cooperative liaison which began in 1933 on the request of the American Occupational Therapy Association, the Council has developed standards for the education of occupational therapists. These were initially adopted by the House of Delegates in 1935, and subsequent revisions have been approved in 1938 and 1949. Recommendations for periodic revisions of standards and initial and continued approvals of curriculums are submitted to the Council by two advisory groups, the Council on Education of the American Occupational Therapy Association and the Advisory Committee on Occupational Therapy Education of the Council on Medical Education and Hospitals. The recently appointed advisory committee consists of nine physician members nominated by national organizations in the fields of chest diseases, general surgery, internal medicine, neurology, orthopedic surgery, pediatrics, physical medicine and rehabilitation, psychiatry, and medical education. In addition, there are three occupational therapist members nominated by the American Occupational Therapy Association and its Director of Education serves as a consultant. Surveys of schools are conducted by joint physician-therapist teams and submitted to the advisory groups which formulate recommendations for final action by the Council. An extensive Curriculum Study Project is being carried out by the American Occupational Therapy Association, to evaluate and further advance educational opportunities in the profession.

TABLE 45.—*American Occupational Therapy Association Statistics for Total Degree and Certificate Student Enrollment and Graduates for the Academic Years 1957-1958 and 1958-1959*

Year	Total Student Enrollment	Graduates*
1957-1958	4,266	561
1958-1959	3,913	581 (estimated)

* Calendar years 1958 and 1959.

As of June 30, 1959, there were 29 approved schools. Statistics for total degree and certificate student enrollment and graduates for the academic years 1956-1957, 1957-1958, and 1958-1959 based upon data submitted to the American Occupational Therapy Association are shown in table 45.

Training for an occupational therapist includes a good general collegiate education coordinated with the professional curriculum in occupational therapy and supervised clinical practice in hospitals. Certificate and degree recognition is available and those so recognized have equal professional status.

Programs leading to a baccalaureate degree are generally of four years' duration and schools offering this curriculum accept qualified high school students and transfer students. Certificate programs are predominantly 18 months in duration and accept students with a baccalaureate degree. However, since universities have individual policies on transfer students, interested undergraduates are encouraged to contact schools of their choice early in their collegiate careers to determine admission requirements for the certificate and/or degree programs in a given school. Tuition in all teaching centers closely parallels college fees. Most courses begin in September or February. Lists of approved schools are available from the Council.

Application by schools for approval of an educational program in occupational therapy should be made to the Council on Medical Education and Hospitals of the American Medical Association. Forms will be supplied for this purpose on request. They should be completed by the administrator of the institution requesting approval. Inquiries regarding career opportunities in the field of occupational therapy and the registration of qualified therapists should be addressed to the American Occupational Therapy Association, 250 West 57th Street, New York 19.

SCHOOLS FOR PHYSICAL THERAPISTS

On the request of the American Physical Therapy Association, the Council developed standards that were adopted by the House of Delegates in 1936. The Council, in cooperation with its advisory groups, the Council on Physical Medicine and Rehabilitation of the American Medical Association and the American Physical Therapy Association, has periodically submitted revised standards to the House of Delegates, which were adopted in 1943, 1949, and 1955. In 1955, the Council on Physical Medicine and Rehabilitation became the Council on Medical Physics, with which there continues close liaison on matters pertaining to physical therapy but which no longer functions in an advisory capacity on physical therapy education. Recommendations for periodic revisions of standards and on initial and continued approvals of curriculums are submitted to the Council by two advisory groups, the American Physical Therapy Association and the Advisory Committee on Physical Therapy Education of the Council on Medical Education and Hospitals. The Advisory Committee on Physical Therapy Education consists of nine physician members who are nominated by national organizations representing the fields of physical medicine and rehabilitation, orthopedic surgery, psychiatry and neurology, internal medicine, pediatrics, general surgery, and medical education. In addition, there are three members who are physical therapists, two nominated by the American Physical Therapy Association and one nominated by the American Registry of Physical Therapists. The educational consultant of the American Physical Therapy Association attends all meetings in this capacity. Surveys of new and existing schools are conducted by joint physician-therapist teams and recommendatory action submitted by the advisory groups to the Council for action. Active liaison with the medical directors, therapist educational administrators, and other members of the teaching faculties in approved schools is being implemented through more frequent periodic surveys.

As of June 30, 1959 there were 39 approved schools. On the basis of data reported to the American Physical Therapy Association, enrollment statistics for the senior class of degree programs and for the certificate programs and the number of graduates for 1957-1958 and 1958-1959 are shown in table 46.

Certificate and degree recognition in physical therapy is available and those so recognized have equal professional status. Most schools offer both degree and certificate programs and either or both recognitions are available depending upon a student's preparatory collegiate education. Certificate programs are usually 12 months in duration, and admit students with two or three years of college or those who have graduated from a nationally accredited school of professional nursing of at least three years' duration. The majority of degree programs are four years in length and admit qualified high school graduates and transfer students. Interested undergraduates are encouraged to contact the school of their choice early since admission and transfer requirements vary. Tuition varies in accord with university fees and the majority of courses begin in September or February. Lists of approved schools are available from the Council.

TABLE 46.—*American Physical Therapy Association Statistics for Degree and Certificate Enrollment and Graduates for the Academic Years 1957-1958 and 1958-1959*

Year and Class	Schools Reporting, No.	Senior (Degree) and Certificates Students Enrolled, No.	Total Graduates, No.
1957 Senior	14	798	750
1957 Certificate	30		
1958 Senior	31	676	718
1958 Certificate	27		

Application for approval should be made to the Council on Medical Education and Hospitals of the American Medical Association. Forms will be supplied for this purpose on request. They should be completed by the administrator of the institution requesting this approval. Inquiries regarding voluntary registration of qualified therapists should be addressed to the American Registry of Physical Therapists, 30 North Michigan Avenue, Chicago 2. Information on requirements for state registration or licensure is available from the Board of Examiners of the states concerned. Inquiries regarding careers in the field of physical therapy should be addressed to the American Physical Therapy Association, 1790 Broadway, New York 19.

SCHOOLS FOR X-RAY TECHNICIANS

The Council has been ably assisted by the American College of Radiology, the American Registry of X-Ray Technicians, and the American Society of X-Ray Technicians in revising criteria for training and evaluating educational programs in x-ray technology. These advisory groups participated in the most recent revision of the standards adopted by the House of Delegates in December, 1955. An increase in duration of the educational program to a minimum of 24 months is currently under consideration to become effective in 1962.

Schools making application for approval are surveyed by state and regional councilors appointed by the American College of Radiology. Radiologists appointed by the College also periodically re-survey approved schools and these radiologists are currently revisiting approved schools. Their tremendous and voluntary contributions of time and experience are a major asset in the program. All data are evaluated by the Committee on Technician Affairs of the American College of Radiology and recommendations submitted to the Council for final action.

As of June 30, 1959, there were 609 schools approved by the Council for training x-ray technicians, which represents an increase of 9% over the 557 approved in 1958. Enrollment for 1958 increased 468 or 11%, to a total of 4,581 students. The training capacity increased 11% in 1958 over 1957 to a total of 5,358. The number of graduates increased 1% to a total of 2,129 in 1958.

The minimum admission requirement is high school graduation. A total of 589 schools (97%) admit students directly out of high school, 14 schools (2%) require one year of college, 5 schools, (1%) require two years of college, and one school accepts only registered nurses.

The length of training in 446 (73%) is 24 months, 12 months in 100 (17%), 18 months in 32 (5%) and varies from 13-48 months in 4%. Seven schools offer two courses of 12 or 24 months' duration. Tuition is required by 213 (35%) and 465 pay students a stipend. Collegiate affiliations have been established by 194 (32%) of approved schools. Students should apply directly to the radiologist-director of an approved school. Lists of approved schools are available from the Council on request.

Applications for approval of schools of x-ray technology should be submitted to the Council on Medical Education and Hospitals of the American Medical Association, 535 N. Dearborn Street, Chicago 10. Inquiries regarding registration of qualified x-ray technicians should be addressed to the American Registry of X-Ray Technicians, Metropolitan Building, Minneapolis 1, Minn.

NATIONAL ACADEMY OF SCIENCES–NATIONAL RESEARCH COUNCIL STUDY OF POSTDOCTORAL FELLOWSHIPS

Postdoctoral fellowships in the medical sciences form an important part of medical education. The Division of Medical Sciences of the National Academy of Sciences–National Research Council have completed a survey of such fellowship programs and their impact on medical education. Dr. Arthur S. Cain Jr., the director of this study, has provided an analysis of the final report of the survey for inclusion in this report on Medical Education in the United States and Canada.

A national survey of postdoctoral fellowships in the medical sciences has been completed by the Medical Fellowship Board of the National Academy of Sciences–National Research Council. The final report of the survey is in the process of preparation and should be available soon. The purpose was to study the impact of fellowships on medical education and research and especially to weigh the appropriateness of current fellowship programs against the implications of recent scientific developments and the needs of academic medicine. Conducted largely by questionnaire, the survey involved some 19,000 physicians and non-physicians who, as past, present, or potential fellows, faculty members and investigators, could provide the necessary information and opinions. Some preliminary information from the survey was included in "Medical Education in the United States and Canada 1957-1958." [19]

As a result of data and conclusions from the survey, the Medical Fellowship Board has recommended termination of its traditional program of National Research Council Fellowships in the Medical Sciences, a program with which it pioneered almost forty years ago. At the same time, based upon its appraisal of the influences now dominating medical education, the Board has proposed a new fellowship program, planned specifically in the interests of academic medicine.

That postdoctoral fellowships play an important role in the education of medical scientists is underlined by the fact that more than 4,500 Doctors of Medicine and Doctors of Philosophy in medical sciences accepted fellowships between 1946 and 1958, under the major national programs alone, to continue their studies and extend their abilities. The number of physicians applying for postdoctoral fellowship awards under these programs for the year 1956-1957 was equal to approximately 10% of the number of physicians graduating from medical schools annually in recent years. Doctors of Philosophy seeking these fellowships in the same year were equal in number to about half of the current annual production of Ph.D.'s in the medical sciences.

Moreover, the survey indicates that fellowships have a potential role far beyond that which is being realized under the present fellowship system. Recent medical graduates indicated a real dissatisfaction with the breadth and depth of their basic scientific backgrounds. Some 40% of 1958 interns and residents in university hospitals want opportunities to eliminate their scientific deficiencies in the physical and biological sciences through postdoctoral programs of a kind that could best be provided by fellowships. Sixty-five per cent of the interns and residents regarded more and better training in scientific investigation as essential to their future careers, regardless of the nature of those careers.

The programs of twenty-two agencies awarding postdoctoral fellowships in national competition were selected for inclusion in the survey. The 4,500 persons who received fellowships from these agencies over the 12-year period 1946-1958 were consulted. Because of ambiguity in the fellowship concept, it was necessary to define very carefully the pattern of the fellowships to be studied. The terms "fellow" and "fellowship" may be used to indicate a wide variety of situations, ranging from assistantships, apprenticeships, research associations, and salary subsidies for part-time teaching, to honors and financial awards to senior scientists for support of their research and leaves for sabbatical study. The Medical Fellowship Board selected for inclusion in the survey those programs that have a direct influence on the development of medical scientists, and that conform in general to a common pattern. To be eligible for one of these fellowships, the candidate must have received a Doctor's degree in medicine or in one of the medical sciences. Essentially full-time application to research and study in a fundamental science of medicine is stipulated. Awards are made for periods of at least six months, usually for a year or more.

In the course of the survey, three trends in medical research and education, and their consequences, have held the attention of the Board. The increasing significance of these trends, together with information coming from the survey, led the Board to the conclusion that its forty-year program of traditional fellowships had accomplished its purpose and should be replaced by a more appropriate program, recognizing the trends and meeting the developing needs of academic medicine.

1. *The traditional and sometimes artificial boundaries between the "Basic" sciences and between the preclinical and clinical sciences are fading.* This process is accelerated as determined individuals gain competence in the concepts and techniques of hitherto unrelated scientific disciplines and bring this competence to bear in their own special fields of interest. Such scientists are as yet few in number, but they suggest a prototype for development consistent with the trend. Recognizing this increasing interdependence of disciplines, some of the medical schools already are experimenting with departmental reorganization and teaching from an inter-disciplinary point of view.

2. *The pattern and character of clinical research are undergoing rapid and dynamic changes.* The best trained clinical scientists are engaging in research on an unprecedented scale, and financial support for their efforts now is abundantly available. "Clinical" research has shifted to include investigations of the fundamental scientific explanations of clinical phenomena. Developments in basic science and their potential for clinical medicine make new demands of clinical investigators and especially of teachers. The clinical scientist must prepare himself according to a new pattern if he is to meet effectively the challenges offered. If he is to play a part in clinical academic medicine, he must become a truly competent physician as well, and the survey indicates that the clinically oriented investigator will not yield on this point. As investigators, physicians and teachers, scientists of this kind can help span the gap between "basic" and "clinical" research. These three roles, equally developed, should ensure the early application to the patient of the impressive advances in fundamental sciences. A new opportunity and a new responsibility thus exist for clinically competent medical scientists.

These responsibilities and opportunities exist equally for the medical scientist in nonclinical fields. The influence of basic sciences on medicine, and medicine's dependence upon them, is so complex that the basic scientist faces a new relationship with the clinician in academic medicine.

3. *A steady attrition in faculty members oriented primarily to the full range of university-medical school obligations is developing in academic departments.* The unprecedented expansion of financial resources for the support of medical research has led frequently to the subordination of primary academic responsibilities to extramurally inspired preoccupation with research. Many faculty members today are lodged in academic halls but look outside their institutions for financial support. Some find it desirable not to engage at all in academic careers. If continued, this trend must necessarily lead to weakening of the new research structure itself, through failure to replace the academic deficit created by this attrition. The inspiration, education, and training of his scientific successors must keep pace with the scientist's research activities; it must not be relegated to a secondary or casual position.

The wisdom of the vast expansion of support of medical research in recent years is not questioned. It is the lack of balance, the rigidity and excesses of the present system, with its dangers to academic medicine, that is disturbing.

The Board in proposing its new fellowship program suggests a qualitative reorientation of the pattern for the scientific development of fellows. Fellowships should influence the young scientists to appreciate the opportunity, indeed the privilege, of meeting the other major responsibilities of academic life in addition to research, although not at the expense of research. The new proposal includes a plan for establishing the fellow ultimately in an appropriate academic position in an effort to restore the balance which has been upset by the depletion of academic faculties.

The very generous support of the John and Mary R. Markle Foundation, which also made the survey possible, and of the Donner Foundation, is providing the Medical Fellowship Board with an opportunity to experiment with its new fellowship proposal through the conduct of a small pilot program. The first fellows appointed under the experiment are at work, and additional appointments will be made during the present academic year. It is hoped that the program will be open for general applications in the very near future. Meanwhile, through this opportunity to experiment, a precise format will be established.

The new fellowships, provisionally designated "National Research Fellowships in Academic Medicine", have these characteristics and qualifications:

1. They are offered to young medical scientists who have special aptitude and interest in careers in academic medicine.

2. Preparation for the assumption of the major responsibilities of university faculty membership is emphasized. The fellow must prepare for leadership in the advancement of scientific knowledge through imaginative and well-conceived research. Of at least equal importance, he must make of himself a competent instructor, able to interpret cumulative scientific experience and theory to the students who will be his academic, scientific and professional successors.

3. In planning to meet these responsibilities, the fellow should recognize the increasing interdependence of the scientific disciplines, the fading of boundaries which have tended to restrict the interests of medical scientists to one or another of the traditional disciplines. During his fellowship period, he should equip himself to draw upon and use the concepts and techniques of those fields of science (e. g., biology, chemistry, physics and mathematics) which have special pertinence to teaching and research in his own area of interest.

4. The National Research Fellowships in Academic Medicine are offered in two categories:

(*a*) One category is open to holders of doctorates in medicine, or in biology, chemistry, physics, mathematics and related scientific fields with special qualifications for, and interest in, productive careers in *basic science departments* of the medical schools.

(*b*) The second category is open to holders of doctor's degrees in medicine who have superior clinical training as well as special qualifications for, and interest in, productive careers in *clinical departments* of the medical schools.

In both categories applicants' programs will be weighed especially for their appropriateness, in the long-range view, for careers in the *academic department* and *scientific area of their interests.*

5. Fellowships in both categories will consist of two phases: A "preparatory" phase of approximately two years, and an "academic" phase of approximately three years.

The "preparatory" period will be devoted to *nonclinical* scientific study including formal course work wherever necessary. Such studies will be planned on an individual basis, determined by the area in which the fellow will make his career, and dictated by the trends which influenced the Board to establish the new program. A definitive program for the development of competence as a competent instructor and original investigator will be included in the program.

In the "academic" phase of three years, the Medical Fellowship Board and a cooperating university will participate in supporting the fellow in a regular academic position. At this point, the fellow will begin to assume the full responsibilities of academic life. The opportunities and program proposed for this phase will be reviewed by the Board with the participating university, the fellow, and his advisors, for its appropriateness to the objectives of academic institutions and the interests of the candidate.

6. These fellowships are intended for the young scientist who is mature and who shows insight and conviction as to his future plans. His ability and determination to chart a course of preparation consistent with his long-range interests and the developing trends in academic medicine will weigh heavily in the selection process. These fellowships are not appropriate for medical scientists who are seeking general educational opportunities and who are not yet certain of the precise nature of their career ambitions. Fellowships comparable to the traditional program of the Academy-Research Council now exist in several modifications under the competent direction of many agencies. These provide excellent opportunities for young scientists while they are discovering their interests and crystallizing their future plans.

The Medical Fellowship Board and the Division of Medical Sciences recognize the difficulties they face in establishing the new program on the basis of these proposals. However, the experience gained thus far in the experiment and the insight, cooperation, and enthusiasm demonstrated by candidates and medical educators alike, justify the hope that their highest expectations will be realized.

THE NATIONAL SCIENCE FOUNDATION

The following résumé of the activities of the National Science Foundation, in so far as they are related to medicine through grants for basic research in the medical sciences, grants for short-term medical research, conferences and symposia supported by the foundation, and fellowships for study at the graduate and postdoctoral level, has been submitted by the Public Information Office of the Foundation.

The National Science Foundation, an agency of the federal government, was established by Congress in 1950 "to promote the progress of science; to advance the national health, prosperity, and welfare; to secure the national defense; and for other purposes." The foundation carries out its mission by supporting basic research in the sciences, programs for improving science education, conferences and symposia on special aspects of science, studies of manpower supply and demand, programs for making scientific information more readily available, and the compilation of data on the national effort in scientific research and development.

Table 47.—*NSF Support of Activities (Research and Conferences) of Interest to Medical Profession*

	Fiscal Year 1958		Fiscal Year 1959	
	No.	Amt., $	No.	Amt., $
Basic medical research grants	21	559,600	122	3,391,250
Short-term research by medical students	17	193,200	30	364,600
Conferences and symposia on subjects of medical interest	1	20,000	1	25,000

Of particular interest to the medical profession are the foundation's grants for basic research in the medical sciences, grants for short-term medical research, and fellowships for study at the graduate and postdoctoral level (table 47).

Basic Research

Grants are made to help competent scientists conduct basic research in the sciences, principally at universities and colleges. Normally, proposals are originated by the scientist and are endorsed and submitted by his institution. Basic research is supported in the mathematical, physical, medical, biological, engineering and other sciences, including to a limited extent, the social sciences. In fiscal year 1959 the congressional appropriation to the foundation for the support of basic research was about $40,000,000. Approximately $20,000,000 was expended in support of the life sciences.

Short-Term Medical Research

In an effort to increase the number of scientists qualified to perform basic research in medical fields, the foundation sponsors a program designed to encourage medical school students to pursue careers in research.

Medical school students constitute one of the largest sources, relatively untapped, of medical research scientists. The medical curriculum is essentially instructional, offering little, if any, opportunity for students to pursue research and become familiar with its methods or challenges. The foundation seeks to introduce medical students to the techniques of basic research by means of its grants to medical schools for the support of short-term research by students during free-quarter periods. Without interfering with the medical curriculum, the program provides opportunities for carefully selected students to determine their interest in and aptitude for research. Student research is conducted under the supervision of qualified members of the medical school staff.

In 1956, the foundation began this program experimentally. In the three years of its operation, the program has expanded considerably and now includes 63 medical schools in the nation. A total of $847,250 has been granted for this purpose.

Conferences and Symposia

The conferences and symposia supported by the foundation provide excellent opportunity for the interchange of information and ideas among experienced investigators, as well as an opportunity for younger investigators to meet and obtain information and advice from some of the world's foremost scientists. Approximately 25 such conferences are supported each year. In FY 1959 there was one such conference of special interest to those in the medical profession and one in 1958 (table 47).

Additional information on the support of research grants in the medical sciences may be obtained from the Division of Biological and Medical Sciences, National Science Foundation, Washington 25, D. C.

Fellowships

The Fellowship Programs of the foundation are designed to strengthen the nation's scientific potential by providing support for advanced training in the sciences directed toward the development of highly qualified scientists and for further study in the sciences directed toward increasing the competence of college science teachers.

Fellowships are offered for graduate study in the physical, medical, biological, and engineering sciences; anthropology and psychology (excluding clinical); certain interdisciplinary fields, and in selected social science fields (in all except Science Faculty Fellowship program). These fellowships are limited by law to citizens of the United States. A fellow may study under his award at any accredited nonprofit American or nonprofit foreign institution of higher education.

Awards are not made to individuals to pursue a course of study designed to prepare them for careers in medical practice or other clinical fields;

nor for support of residency training or similar work leading to qualification in a clinical field. Applications are accepted, however, from students who intend to obtain advanced training in one of the medical sciences directed toward a career in research. An individual who holds a degree such as M.D., D.D.S., or D.V.M. and desires to continue training for a career in research is eligible to apply for a postdoctoral award provided he can present an acceptable plan for study and research.

Six fellowship programs are offered—the graduate, cooperative graduate, summer fellowships for graduate teaching assistants, postdoctoral, senior postdoctoral, and science faculty. The graduate program is open to students studying for masters or doctoral degrees in science. The three predoctoral levels, first-year, intermediate-year, and terminal-year, carry base stipends of $1,800, $2,200, respectively, with allowances for travel and dependents. Approximately 1,100 graduate fellowships were offered during 1959. The cooperative graduate program was initiated in fiscal year 1959 and differs from the older graduate program in certain operational aspects. A stipend of $2,200 is associated with these awards. Approximately 1,050 awards were offered in 1959. The graduate teaching assistants program, introduced in fiscal year 1959, offered support during the summer months in 1959 to 580 students.

The postdoctoral program is available to those who have earned a doctoral degree or have had research training and experience equivalent to that represented by such a degree. The stipend is $4,500 with allowances for travel and dependents. These awards are made semiannually, and 194 were offered in 1959.

The objective of the senior postdoctoral program is to provide senior, established scientists an opportunity to increase their competence as investigators in their own or related fields. These scientists should have held their doctoral degree for a minimum of five years. A salary-matching stipend is awarded, up to a maximum of $12,000. Approximately 75 such fellowships are awarded each year.

To increase the effectiveness of the teaching of college science teachers, the foundation awards annually science faculty fellowships to teachers with three years college teaching experience and plan to continue teaching. A salary-matching stipend is given up to a maximum of $12,000; 302 such fellowships were offered in 1959.

During fiscal year 1959, 50 fellowships were awarded in the medical sciences. There were 11 graduate, 10 cooperative graduate, 6 teaching assistants, 10 regular postdoctoral, 4 senior postdoctoral, and 9 science faculty fellowships. In addition, 114 were offered awards in biochemistry, 20 in biophysics, 30 in general biology, 57 in genetics, 42 in microbiology and 210 in zoology. These are the classifications of the applicants themselves.

Additional information on the various fellowship programs of the National Science Foundation may be obtained from the Fellowships Section, Division of Scientific Personnel and Education, National Science Foundation, Washington 25, D. C.

EDUCATIONAL VALUES OF THE GRANTS AND TRAINING AWARDS PROGRAMS OF THE UNITED STATES PUBLIC HEALTH SERVICE

Because of their rapid growth since 1945 and their contribution and impact on undergraduate medical education, graduate education and training, and on the research activities and potentials of medical schools, any current report on Medical Education in the United States would be incomplete without presentation of the Educational Values of the Grants and Training Awards Programs of the United States Public Health Service. The following information reviewing the current status of these programs was prepared and submitted by the Public Health Service, United States Department of Health, Education, and Welfare.

Several programs of the United States Public Health Service are of interest to the field of medical education. The programs of grants and training awards in the medical and related sciences help add to the nation's supply of trained personnel in the life sciences. These programs are of several types: (1) research fellowships, (2) training grants and traineeships, (3) research grants, and (4) health research facilities construction grants. In addition, the Public Health Service administers traineeship programs for professional nurses and public health personnel. Finally, the Service conducts a number of intramural training programs in its own hospitals and research centers.

The research grants and awards programs are administered through the Public Health Service's principal research bureau, the National Institutes of Health. Although research is conducted at the NIH laboratories in Bethesda, Md., by far the major portion of the annual appropriations—some two-thirds this year—help support research studies and training in nonfederal institutions. In fiscal year 1959, grants for these purposes amounted to 200 million dollars, about 50% of which supported activities in the medical schools.

A wide range of medical and biological investigations and of training activities is aided by the Institutes: National Cancer Institute, National Heart Institute, National Institute of Allergy and Infectious Diseases, National Institute of Arthritis and Metabolic Diseases, National Institute of Dental Research, National Institute of Mental Health, and National Institute of Neurological Diseases and Blindness. In addition, the NIH's Division of General Medical Sciences administers a program of grants for training and research studies not falling within the categories of the seven Institutes. The Division of Research Grants provides central review and processing for all the grants programs of the National Institutes of Health, has important functions with regard to research fellowship programs, and administers grants for the construction of health research facilities.

Nine national advisory councils, established by law and composed of nonfederal leaders in medical science, education, and public affairs, review all grant applications within their respective areas and recommend action to the surgeon general of the Public Health Service. The councils are assisted by nearly 40 study sections—panels of outstanding specialists, mostly nonfederal—who provide initial review of research project applications for scientific merit. In addition to these specific functions, the councils and study sections, as well as various special committees and review groups, contribute overall guidance to the research grant and training activities.

In fiscal year 1959, approximately 8,500 people in nearly 400 schools and research centers were aided through the training grants and fellowships programs. In the same year, an estimated 9,250 research projects were supported through grants totaling about $142,000,000. These grants provide indirect educational and teaching values.

These, and other kinds of Public Health Service programs of interest to medical education through both direct and indirect educational relationships, are presented in the following brief summaries. (Further information may be obtained from the Division of Research Grants, National Institutes of Health, Bethesda 14, Md.)

Research Fellowships

Research fellowships are intended to increase the number of scientists qualified to carry on independent research. Seven types of fellowships are presently available:

1. Predoctoral research fellowships are awarded to students with a bachelor's degree or equivalent, for the pursuit of graduate research training in the fields related to the health sciences. Stipend rates are $1,800, $2,000, and $2,200 for the first, second, and third years, respectively. Allowances for dependents, travel, and tuition are added to the stipend. An allowance of $250 may be paid to the sponsoring institution to defray unusual expenses.
2. Postdoctoral research fellowships are awarded to qualified persons holding a Doctor's degree in medicine, dentistry, or related fields. Stipend rates are $4,500, $5,000, and $5,500 for the first, second, and third years, respectively. Allowances for dependents, tuition, and travel are added to the stipend.
3. Special research fellowships are awarded to qualified candidates who have demonstrated unusual competence in research or who require specialized research training. The stipend, including necessary allowances, is determined at the time of the award.
4. Student part-time research fellowship grants are awarded to schools of medicine, dentistry, nursing, and public health. The awards are designed to give students in the health sciences an opportunity to explore the research field in the hope that many of those supported will enter into full or part-time research careers. Units of $600 are provided for part-time research work during the school term or full-time research work for two months during any time when curriculum work is not scheduled for the student.
5. Senior research fellowship grants are awarded to schools of medicine, dentistry, and public health in support of competent scientists who wish to conduct research and teaching in the preclinical sciences. These fellowships provide support between the completion of postdoctoral training and the time of eligibility for appointment to permanent or higher academic posts. The awards are made for five-year periods, are renewable, and provide for salary plus partial research expenses not exceeding $2,000. Senior research fellows may also apply for additional support for their research needs.
6. Post-sophomore research fellowship grants are awarded to schools of medicine and dentistry for support of students who wish to obtain research training prior to completion of their professional degrees. Participants must be willing to drop out of regular courses for one, two, or three years. The stipend is set by the school in amounts not to exceed $3,200 annually. Allowances for dependents and tuition are added to the stipend. A special allowance of $250 may be paid to the sponsoring institution to defray unusual expenses.
7. Foreign research fellowships are awarded to a limited number of scientists who wish to study in United States laboratories. The purpose of the program is to provide an opportunity to strengthen medical research by mutual exchange of research methods, scientific philosophy, and cultural values. Nominations are made by respective national research organizations in each western European country. Candidates must have (*a*) completed a doctoral degree in one of the medical or related sciences and demonstrated proficiency in research, (*b*) made satisfactory arrangements with the laboratory in the United States where training *will* be obtained, and (*c*) acquired a workable reading and speaking knowledge of the English language. Scientists will be brought to the United States on an exchange visitor's visa, which requires return to the homeland for a period of at least two years at the end of the training period. The basic stipend is $4,500 per year. Dependency, travel, and certain other allowances are added to the stipend.

Training Grants and Traineeships

Training grants are intended to augment the nation's supply of qualified scientific investigators by assisting in the establishment, expansion, and improvement of training and instructional programs in universities and other institutions. Aid to the institution is provided by grants in two general classes—undergraduate and graduate.

1. Undergraduate training grants are awarded to schools of medicine, dentistry, nursing, and public health to assist in developing expanded and better integrated undergraduate instruction relating to the prevention, diagnosis, and treatment of cancer, mental illness, and cardiovascular diseases. It is the responsibility of the institution to determine the most appropriate use of the funds.

2. Graduate training grants are awarded by all the Institutes and by the Division of General Medical Sciences to public and private nonprofit institutions interested in providing special training for researchers, teachers, and prospective practitioners interested in public service. Funds may be used to improve facilities and to provide salaries for faculty and staff, stipends for trainees and necessary supplies and materials.

Special new training grants programs are being established also in fields of special need through the Division of General Medical Sciences and other NIH units. For information on these programs, write either to the Division of General Medical Sciences, NIH, or to the Associate Director for Training, NIH.

Traineeship awards are intended to increase the number of investigators by encouraging advanced training in specialized areas of medical research. Examples of interest are the neurological diseases, ophthalmology and sensory diseases, diagnosis and treatment of cancer, and arthritis, diabetes, and other metabolic diseases.

Regular or special traineeships are awarded directly to American citizens and to aliens who have signed a Declaration of Intent. A doctoral degree in health fields, including related biological and behavioral sciences, is also a prerequisite. Traineeships are available through the National Cancer Institute, the National Institute of Arthritis and Metabolic Diseases, and the National Institute of Neurological Diseases and Blindness. The National Heart Institute and the National Institute of Mental Health provide traineeships under training grants awarded to institutions for this purpose.

The regular traineeship award carries a stipend level that begins at $3,800 per year (with the exception of the National Institute of Arthritis and Metabolic Diseases traineeships, which start at $4,500) and includes dependency allowances and certain travel allowances. No allowances are made for tuition or supplies.

Special traineeships are awarded by the National Institute of Neurological Diseases and Blindness and the National Institute of Arthritis and Metabolic Diseases in varying amounts to qualified individuals who possess unusual competence for training or who require specialized training for a specific problem. The trainee may study at the institution of his choice. The stipend is determined by the cost of training and by the particular qualifications of the applicant; it ranges between $6,500 and $17,500.

Public Health and Professional Nurse Traineeships

The public health traineeship program of the Public Health Service supports graduate and specialized public health training for individuals who have completed their basic professional education and plan employment in the field of public health. Awards are made directly by the Public Health Service, by schools of public health, and by nursing schools that prepare graduate nurses for beginning positions in public health. These traineeships are awarded to physicians and to members of other professions who engage in public health work, such as dentists, veterinarians, nurses, sanitary engineers, health educators, sanitarians, nutritionists, and others. The traineeships include payment of stipends, tuition and fees, and certain travel expenses. About 650 traineeships are awarded each year, approximately half of which support public health training for nurses.

A limited number of similar traineeships are available to professional personnel who are or plan to be engaged in the prevention and abatement of community air pollution. These traineeships support specialized training related to the effects, extent, assessment or control of air pollution.

Applications for public health or air pollution traineeships may be obtained from any of the regional offices of the Public Health Service or from the Chief, Division of the General Health Services, Bureau of State Services, Public Health Service, Washington 25, D. C.

Another Public Health Service program provides traineeships for professional nurses who are interested in teaching, supervisory, and administrative positions. Stipends of $2,400 to $3,600 plus tuition, certain travel fees, and dependency allowances of $360 are available through schools of nursing. This program is administered by the Division of Nursing Resources, Bureau of Medical Services.

Research Grants

Research grants are made to universities, medical schools, hospitals, laboratories, and other public or private institutions and to individuals for support of research in health, medicine, and allied fields. The major objectives are: to expand medical and biological research in scientific institutions throughout the country, and to stimulate new investigations in fields needing exploration. The program also provides training, indirectly, for the scientific personnel engaged in the research work. The funds provide for salaries, equipment, supplies, travel, overhead, and certain other expenses.

Each institute makes grants for research within its area of interest, and a general NIH appropriation supports studies outside the scope of the seven Institutes.

This year there will be some 9,250 research grants awards in every part of the country. Some 5,000 or so professional papers will be published by research grantees in a wide variety of journals as a result of this work.

Field investigation grants, awarded by the National Cancer Institute, support developmental research, community studies, and surveys that will contribute to the prevention, control, diagnosis, and treatment of cancer in the general population.

The Public Health Service also administers grants for special research projects. Among these are investigations of the health aspects of air and water pollution, projects for the development and utilization of hospital facilities and resources, and studies to improve nursing education and service. The projects are administered by the Division of General Medical Sciences, NIH, for the sponsoring divisions in the Bureau of State Services (the Division of Sanitary Engineering Services and the Division of General Health Services) and in the Bureau of Medical Services (the Division of Hospital and Medical Facilities and the Division of Nursing Resources).

Health Research Facilities Grants

Under the Health Research Facilities Act of 1956, the Congress authorized a program to assist in the construction of laboratories and other facilities for the conduct of health research. The program provides grants-in-aid on a matching basis to public and private nonprofit institutions. The amount of federal funds awarded may not exceed 50% of the total costs of the research portion of the facility, and the remaining sum must be provided from nonfederal sources. Each year since 1956, the sum of $30,000,000 has been appropriated for this program, and several hundred awards have been made to institutions in all parts of the country. As a result, many new research facilities are now in operation that would not otherwise have been made possible.

Training for Public Health Service Careers

The Public Health Service, in its widespread and diversified programs, offers many career opportunities to competent physicians. Training is provided in various areas of medicine, including patient care, clinical research, basic laboratory research, epidemiology, preventive medicine, quarantine duty, foreign service, and public health administration.

Most of the Service's physicians are officers in the Commissioned Corps, which has served this country with distinction since 1873. A young physician or medical student may enter the Corps (1) through the Commissioned Officer Student Training and Extern Program (COSTEP), (2) as an intern upon graduation from medical school, and (3) as a medical officer after nonservice internship.

Clinical assignments are available in most of the Service's 16 general and special hospitals and in many of its 56 hospitals for American Indians and Alaskan natives. Postgraduate medical education in the teaching hospitals is conducted by chiefs of service (who are certified or eligible for certification by their specialty boards), with the assistance of well-qualified personnel and outstanding consultants from local hospitals and medical schools. Approved internships are also offered in dentistry, dietetics, and pharmacy.

Rotating internships consisting of assignments planned to round out a young physician's education are available in the Service's hospitals at Baltimore, New Orleans, New York, Norfolk, San Francisco, Seattle, and Boston. The schedule provides four months of medicine, four of surgery, two of pediatrics, and two of obstetrics. Mixed internships, available at the Public Health Service hospital in Boston, provide six months of medicine and six of surgery.

In addition to the usual educational requirements, the applicant for appointment as a medical intern must: (1) be in good health, (2) be an American citizen, and (3) submit an application for a reserve commission in the Public Health Service. Those who have satisfactorily completed the year's internship may apply for continuing assignment with the Service. They are eligible to take the examination for appointment in the regular corps.

In addition to the internships, Public Health Service hospitals offer approved residency training in the following specialties: surgery, general practice, internal medicine, orthopedics, urology, anesthesiology, dermatology and syphilology, ophthalmology and otolaryngology, pathology, radiology, and psychiatry. The National Institutes of Health's Clinical Center, a 500-bed research hospital at Bethesda, Md., offers residency training in internal medicine, neurology, ophthalmology, pathology, psychiatry, and radiology. Residents are usually selected from the Commissioned Corps.

Through the Commissioned Officer Residency Deferment (CORD) program, Public Health Service offers qualified physicians the opportunity to obtain deferment from the military service under the Universal Military Training and Service Act. Physicians are commissioned in the Reserve Corps of Public Health Service and deferred from active duty to obtain residency training in essential specialty fields. After completion of training, participants must serve their obligatory time with Public Health Service. No additional military service is required.

The program known as COSTEP provides employment for a limited number of medical and dental students during the vacation months for duty at Public Health Service hospitals, research laboratories, and other facilities. Appointments are offered to students who will have completed their sophomore year of professional education by July 1 and are interested in becoming reserve officers in the Commissioned Corps.

Information concerning employment in the Public Health Service may be obtained from the Surgeon General, United States Public Health Service (P) Washington 25, D. C.

Visiting Scientist Program

The visiting scientist program is a flexible arrangement for inviting outstanding American and foreign scientists to utilize the laboratory and clinical research resources of the National Institutes of Health. Two classes of appointment are available—"visiting scientist" and "research associate in the visiting scientist program." Participants must have a doctoral degree or the equivalent background, at least six years of postgraduate experience, and exceptional ability in a specific research problem. The salary range is from $5,400 to $12,600 a year. The purpose of the program is to increase the utility of the National Institutes of Health as a national resource and to strengthen interrelations with the broader scientific community.

Conferences and Seminars

To encourage early and adequate exchange of information among investigators, numerous conferences, seminars, and symposiums are supported in connection with the grants and training programs. Many of the meetings are initiated and sponsored by the advisory study sections of the Division of Research Grants.

In addition, the Institutes and Divisions, separately or as a whole, present lectures, seminars, and clinical conferences. Frequently there is active participation by faculty members of universities and medical schools, staffs of other research centers and Public Health Service hospitals, physicians in private practice, and other leaders in the medical sciences.

CONTRIBUTIONS OF THE OFFICE OF VOCATIONAL REHABILITATION TO MEDICAL EDUCATION AND RESEARCH

Since 1954 the Office of Vocational Rehabilitation, under authority of the Vocational Rehabilitation Act, has offered direct and indirect aid of five types to medical education and research. The following summary of various grant programs administered by the Office of Vocational Rehabilitation which have an impact on medical education has been prepared by its administrative staff for the Education Number of The Journal.

The Office of Vocational Rehabilitation, Department of Health, Education, and Welfare, offers direct and indirect aid to medical education. Direct aid is available in the form of long-term teaching grants and short-term course or institute grants to the schools. Less direct but significant support is provided through research grants, research fellowships, and traineeships. These five types of aid, made possible under authority of the Vocational Rehabilitation Act of 1954, may be summarized as follows:

1. Teaching grants assist medical schools in initiating, expanding, or improving teaching in the rehabilitation phases of medicine. The number of medical schools receiving teaching grants has increased from 6 in 1956 to 25 during the 1958-1959 academic year. Averaging from $15,000 to $25,000, the grants are intended to provide part of the costs of the teaching program. Generally, they cover the salary of a faculty member coordinating the program, payment for the part-time services of supporting staff, and the purchase of instructional equipment or materials. The duration of these grants is one year with provision for reapplication by the institution for continued support.

2. Grants are made for institutes or short-term training courses designed to stimulate interest in rehabilitation or to increase the specialized knowledge of rehabilitation philosophy and methods. In 1958-1959, courses were conducted in geriatric rehabilitation, neuromuscular facilitation techniques, esophageal speech, aphasia, and rehabilitation in surgical conditions. One course was held for physicians working as medical consultants in state vocational rehabilitation agencies on administrative problems encountered in such consultation, and others are planned for the future. In 1958-1959, courses in prosthetics and orthotics reached over 1,000 physicians and surgeons, physical and occupational therapists, prosthetists, orthotists, and personnel from State vocational rehabilitation agencies. Since 1954, courses in rehabilitation of the upper or lower extremity amputee and in functional bracing of the upper extremities have reached about 3,400 physicians and associated personnel.

3. Traineeship grants in medicine serve the purpose of increasing the nation's supply of qualified physiatrists. They were given during the past academic year to 30 institutions offering approved residency programs in physical medicine. From this source the institutions, in turn, awarded traineeships to individual physicians. The number of physicians receiving this type of support has increased from four on July 1, 1955, to 105 on June 30, 1959. In these four years traineeship assistance has increased from about $287,500 in 1956 to over $739,000 in 1959.

Office of Vocational Rehabilitation funds have also been used in several institutions to provide part-time training in rehabilitation for residents in internal medicine, orthopedics, urology, neurology, neurosurgery, and psychiatry.

4. Research and demonstration grants are available for the partial support of projects aimed at developing more effective methods and techniques for the vocational rehabilitation of disabled persons. The grants are recommended for approval by the National Advisory Council on Vocational Rehabilitation which is composed of medical, educational, and scientific members who are established authorities in fields concerned with vocational rehabilitation. Sponsors of research and demonstration projects must pay part of the total cost of the project, but there is no specific matching requirement. It is expected, however, that contract authority will become available permitting payment of the full cost of selected projects.

Projects are being encouraged in the following categories: (*a*) studies designed to determine physiological changes which occur during treatment and retraining in physical rehabilitation; (*b*) the development of new and improved diagnostic techniques; (*c*) investigations to elucidate the dynamics of individual and group motivation as a factor in success or failure of physical medicine procedures; and (*d*) projects for developing quantitative methods for evaluating functional capacities of disabled individuals.

As the Research and Demonstration Grant Program has developed, an increasing number of projects are being carried on by medical schools, hospitals, and medically oriented organizations. In addition, many projects sponsored by other types of agencies are under medical supervision.

5. Research fellowships may be awarded to assist qualified candidates to pursue advance training for research or to undertake a research project which holds promise of advancing knowledge of the vocational rehabilitation of disabled persons. Three types of fellowships are available: predoctoral, postdoctoral, and special. The awards are made on an annual basis and are subject to a limitation of two years.

The programs of the Office of Vocational Rehabilitation in aid to medical education are based on long-standing practices of co-operation with state and local agencies and educational institutions. National advisory committees play a major role in the administration of the office's educational grants program. These committees, composed of leaders in the educational, research, and administrative phases of the various rehabilitation disciplines, have helped to formulate the policies and basic principles which govern the grant programs for medical education. Academic freedom for the institutions and individuals receiving grants is a primary consideration. The intent of Congress, the recommendations of the advisory committees, and the traditions and experience of the Office of Vocational Rehabilitation provide maximum safeguards for that freedom. In carrying out the over-all program, every effort is made to insure the widest distribution of funds, taking into consideration the number and quality of the projects and the available resources.

MEDICAL EDUCATION FOR NATIONAL DEFENSE

The following information on the status of Medical Education for National Defense, current to July 1, 1958, was submitted by the office of the national coordinator of the program.

The Medical Education for National Defense (MEND) program is at present active in 55 medical schools in the United States, and 15 additional schools have been selected for affiliation effective Oct. 1, 1959. Requests for affiliation have consistently been in excess of the program's ability to expand, and a waiting list for affiliation is maintained.

The 55 schools now taking part in the program are Albert Einstein, Baylor, Boston University, Bowman Gray, Buffalo, California (San Francisco), UCLA, Cincinnati, Colorado, Columbia, Cornell, Creighton, Duke, Emory, Georgetown, George Washington, Howard, Illinois, Indiana, Iowa, Kansas, Louisiana State, Louisville, Marquette, Maryland, College of Medical Evangelists, Meharry, Miami, Michigan, Mississippi, Nebraska, State University of New York (Syracuse), NYU, North Carolina, Northwestern, Ohio State, Oklahoma, Pennsylvania, Pittsburgh, Puerto Rico, Rochester, Stritch, Temple, Texas (Galveston), Texas (Southwestern), Tufts, Tulane, Vanderbilt, Vermont, Medical College of Virginia, University of Virginia, Washington University (St. Louis), University of Washington (Seattle), Western Reserve and Wisconsin.

The schools which have been selected for affiliation effective Oct. 1, 1959, are Albany, Arkansas, University of Chicago, Hahnemann, Jefferson, Minnesota, Missouri, New York Medical College, South Dakota, Southern California, Tennessee, Utah, Wayne State, West Virginia, and Woman's Medical College of Pennsylvania.

MEND is a function of the Committee on MEND of the Association of American Medical Colleges; it is endorsed by its parent organization, by the American Medical Association Council on Medical Education and Hospitals and the Council on National Defense, and by medical officials of the Department of Defense, Army, Navy, Air Force, Public Health Service, Atomic Energy Commission, and the Office of Civil and Defense Mobilization.

The purpose of the program is to encourage the teaching of military and disaster medicine by regular faculty members of the nation's medical schools. The emphasis throughout is on medical, rather than military, aspects. Nothing is mandatory; each faculty is free to reject any part of the program which it may deem inconsistent with the local principles of medical education. Through successful operation of the MEND program, the problem of national preparedness in medical education can be solved by interested faculty members on a local basis and under local control rather than through such methods as the establishment of a federal medical school or through direct federal intervention in curricular content.

Every year MEND sponsors a series of symposia, which are conducted by federal medical personnel for the benefit of faculty members of medical schools. During 1958-59, five symposia were held. Their topics, the agencies conducting them and their locations were: "Infectious Disease Problems," Walter Reed Army Institute of Research, Washington, D. C.; "Medical Operations and Research in Climatic and Environmental Extremes," U. S. Naval Medical School, Bethesda, Md.; "Research and Development in Aviation and Space Medicine," USAF Aero Medical Laboratory, Wright-Patterson Air Force Base, Dayton, Ohio; "Nutrition under Wartime or Disaster Conditions," U. S. Army Medical Research and Nutrition Laboratory, Denver, Colo.; and "Radiation Health Problems," Division of Radiological Health, Public Health Service, Washington, D. C. An Average of 85 medical school faculty members attended each of the symposia. Every year MEND also conducts an Orientation Tour for deans and MEND coordinators of schools newly affiliated with the program. The tour is designed to introduce them to current medical research, practices, and facilities in the federal services.

Activities at the 55 schools have included special lectures, conferences, and demonstrations in the following subjects: surgery of trauma, wound ballistics, war wounds, radiobiology, defense measures against chemical and biological warfare, aviation medicine, management of mass casualties, civil defense responsibilities of the medical profession, infectious disease problems in disaster conditions, and others. Several large-scale exercises have been conducted by the schools in cooperation with local civil defense authorities, using the 200-bed emergency hospitals provided by OCDM.

The office of the national coordinator of MEND is located in the Bureau of Medicine and Surgery, Department of the Navy, Potomac Annex, Washington 25, D. C.

NATIONAL DEFENSE AND MEDICAL EDUCATION

SELECTIVE SERVICE SYSTEM

The following information, current as of July 1, 1959, has been submitted by the Selective Service System National Headquarters.

The responsibility for primary classification of registrants rests with Selective Service local boards. If a person or his employer (college, medical school, or hospital) has requested his deferment and he has been classified as available for military service, the person or his employer may, within 10 days of the mailing of the notice of classification, file an appeal. The appeal will be reviewed ordinarily by the appeal board having jurisdiction where the registrant's local board is located, but it may be transferred for review to the appeal board having jurisdiction in the area where the registrant is working or attending college if this is requested in writing when the appeal is made. If the state appeal board should sustain the classification, the registrant or his employer may, if there is a dissenting vote in the appeal board, file a written request with the local board to have the decision appealed to the President. If there is no dissenting vote, the state or national director of Selective Service may appeal the case to the President.

The Undergraduate College Student Certificate (SSS form 109) will be used for undergraduate students entering institutions of higher learning. The Graduate or Healing Arts College Student Certificate (SSS form 103) will be used for postgraduate students entering medical school in furnishing the Selective Service local boards with information regarding registrants who are enrolled as students in these institutions. These forms should be submitted to the local boards by the educational institution on request of the registrant. However, the mere filing of such a form does not constitute a request for occupational deferment, since, in order to establish the right of appeal as an interested party, a written request from the college or employer for occupational deferment must accompany the form. The registrant has the right of appeal if exercised in the prescribed 10 days. He may make his appeal informally in writing.

Eligibility for Consideration for Deferment

The law empowers the President to provide for the deferment of any person whose deferment is equitable and in the national interest. Furthermore, it is the sense of Congress that provision should be made for the annual deferment from training and service of premedical, predental, and allied preprofessional students in numbers equal to those at present (1950) in attendance at colleges and universities as outlined in the general student deferment program.

Sections 1622:15 and 1622:25 of the Selective Service Regulations specify the conditions under which students pursuing programs of higher education may be considered for deferment. Within these specified requirements, students of the healing arts are considered for deferment in the same manner as students pursuing other undergraduate or graduate courses at colleges, universities, and similar schools.

Any student not previously deferred who is pursuing a full-time course of study is entitled to a single period of statutory deferment, class 1-S, until the end of the academic year. Such deferment does not preclude the possibility of later deferment in class 2-S. Students whose activity in study, research, medical, or other endeavors is found necessary to maintenance of the national health, safety, or interest may be deferred in class 2-S until completion of their college training, provided they maintain satisfactory scholastic records. A student who is deferred for study extends his liability for military training and service up to his 35th birthday instead of his 26th, as prescribed for registrants who have never enjoyed a deferment.

In selecting a student for deferment in class 2-S, the Selective Service local boards may, at their discretion, be guided either by the score made by the student on the Selective Service College Qualification Test or by his record of academic performance. The college qualification test is given for the Selective Service System by the Science Research Associates, Inc., of Chicago. At present, in order to be eligible for deferment on the basis of this test, an undergraduate student must make a score of 70 or more. SSS Form 108 has been prescribed for furnishing to the local board the score made on this test. This score is confidential and may be divulged by the local board only to the registrant or to one holding his written consent.

To qualify for deferment on the basis of academic performance, the nonprofessional student must have maintained the following standing among the male members of his class: freshman year, upper one-half; sophomore year, upper two-thirds; and junior year, upper three-fourths. A student accepted for admission to medical school after July 1, 1951, for the class next commencing may be deferred, provided that, during his last full-time year at college or university, he was ranked among the upper one-half of the male members of his class or had a score of 70 or more on the Selective Service College Qualification Test.

A student accepted for admission by a graduate school after July 1, 1951, as a full-time student for the class next commencing may be deferred provided that, in his last full-time academic year in a college or university, he achieved a scholarship standing among the upper one-fourth of the male members of his class or scored 80 or more on the qualification test and provided that the graduate school certifies that he is meeting the degree requirements. Decisions concerning deferment of American students enrolled in foreign universities, including medical students, are the responsibility of the local boards. The local board may accept or reject any claims or evidence presented for deferment.

Status of Interns and Residents

The Selective Service System has always recommended the deferment of graduates of medicine to complete one year of internship training. Selective Service has stated that men, to be given favorable consideration for deferment to complete a residency or more than one year of internship, should be absolutely essential to the operation or maintenance of the hospitals where they are employed or that they be among those selected by the Assistant Secretary of Defense, Health and Medical, to participate in the Armed Forces Reserve Medical Officer Commissioning and Residency Consideration Program or by the Surgeon General of the United States Public Health Service and recommended for specialty training necessary in the staffing of hospitals of the Armed Forces or the United States Public Health Service. The Selective Service System is of the opinion that there is a sufficient number of young physicians who have satisfied their military liability or who are physically disqualified for military service to satisfy the requirements of the hospitals for residents and to provide for specialty training for civilian needs.

The Director of the Selective Service System has agreed to recommend to the Selective Service local boards the deferment of the men selected by the Department of Defense and by the United States Public Health Service, the latter not to exceed 300 as an over-all total for the Public Health Service. It is expected that these programs may be continued from year to year dependent upon the needs.

All young physicians participating in these programs must be commissioned in a Reserve component of the Armed Forces or the Public Health Service and agree to serve two years active duty following the completion of such training. The request for deferment is to pass from the individual to the Department of Defense, attention of the Assistant Secretary of Defense, Health and Medical, or the Surgeon General of the United States Public Health Service. Then, if recommended, it will be forwarded through national headquarters of the Selective Service System to the respective local boards of that system.

Those graduates of medicine who accept a commission in the medical corps reserve of an armed force will not be used, according to present Selective Service policy, to fill a regular call; therefore, such young men who are accepted in the Armed Forces Reserve Medical Officer Commissioning and Residency Consideration Program and who accept reserve commissions will be classified by their Selective Service local boards in a class indicating that they are members of the reserve forces. Should it become necessary for the Department of Defense to place with Selective Service a special call for doctors of medicine, such men will then be given consideration for deferment from active duty for such period of time necessary to complete their training.

A young physician who has established himself in a community where he has been found by his local board essential to the maintenance of an adequate medical service in that community may be deferred by his Selective Service local board or such a physician may be deferred for teaching, research, or Public Health work when these are considered by the local board to be essential in the national interest.

For the academic year 1958-1959, the Public Health Service has arranged certain research grants for students who have completed two years in medicine. These grants will be for one year, and the deferment of these special men will be requested by the individual registrant and recommended by the surgeon general, United States Public Health Service.

Status of Faculty Members

No policy has been announced by the Selective Service System on the granting of deferment to faculty members, except that teachers of medicine have been mentioned in a Selective Service Operations Bulletin as being in a critical occupation to which local boards should give special consideration. It has been recommended that as a general policy, essential members of the medical, dental, and veterinary faculties be held in their teaching positions until such time as replacements are found. This recommendation applies especially to persons in the basic science departments. This policy is not a blanket recommendation for deferment from military service for all teachers. Part-time teachers, who devote only a small portion of their time to teaching, will be expected to enter the military services. The President is also directed to establish a national advisory committee to advise the Selective Service System and to assist state and local advisory boards in selecting the needed medical, dental, and allied personnel.

Expiration of the "Doctor-Draft" Law

The August, 1957, issue (vol. 7, no. 8) of Selective Service carried a statement regarding the expiration of the "Doctor-Draft" law and the new legislative provisions for "Specialists' Service." Because of its importance from the standpoint of medical education as well as its implication in medical practice, this statement is presented in full in the following paragraphs.

"Doctor-Draft" Law Expires; New Legislation Provides for Specialists' Service

Amendments to the Universal Military Training and Service Act, as amended, adopted in June, 1957, replace the former "Doctor-Draft" law and provide for meeting the requirements of the armed forces for medical, dental, and allied specialists until June 1, 1959. Under the new amendments only those specialists who are otherwise liable as regular registrants are subject to induction under the Selective Service law.

The old "Doctor-Draft" law under which medical, dental, and allied specialists had been liable since 1950 expired July 1, 1957. It had placed liability for service on older doctors, dentists, and allied specialists, at one time up to the age of 51.

One of the principal effects of the new amendments to the basic Selective Service Law is to limit liability of doctors, dentists, and allied specialists to age 35 for those deferred on or after June 19, 1951, and to age 26 for others. Public Law 85-62, which amends the basic Selective Service Law with respect to these specialists, was signed by the President on June 27, 1957. By placing medical, dental, and allied specialists under the same provisions of law and regulations as other registrants with respect to the upper limit of the age of liability, the 1957 amendments relieve from liability under the Universal Military Training and Service Act, as amended, any such specialist over the age of 32 on the date the amendments became effective—July 1, 1957. This is true because in order to have acquired extended liability under the June 19, 1951, amendments, a registrant not only must have been deferred on or after that date but also must not have attained the 26th anniversary of his birth by that date. Any man who was 26 on June 19, 1951, would, on July 1, 1957, have been 32 years old.

The amendments in addition provide that:

1. No person in the medical, dental, and allied specialist categories shall be inducted if he applies for an appointment as a reserve officer and is or has been rejected for such an appointment on the sole ground of physical disqualification.
2. The President may order to active duty for not more than 24 consecutive months any member of a reserve component who is such a specialist, who is under 35, and who has not performed at least one year of active duty in the armed forces.
3. Any such person called or ordered to active duty from a reserve component of the armed forces, and who serves on active duty as a specialist for 12 months or more, shall on release from active duty or within six months be given an opportunity to resign the commission unless he is otherwise obligated to serve in active training and service in the armed forces or in training in a reserve component by law or contract.
4. Any physician or dentist qualified for a reserve commission shall, so long as need for his services exists, be given an opportunity to volunteer for active duty of not less than 24 months.
5. The President may prescribe rules and regulations for the selection or induction of persons by age group or groups and for the selection and induction of persons qualified in needed medical, dental, or allied specialist categories pursuant to requisitions submitted by the Secretary of Defense.
6. Qualified specialist aliens liable for induction shall not be held ineligible for appointment as commissioned officers solely on the grounds that such alien specialists are not citizens or have not declared their intention of becoming citizens.
7. Any qualified person who is liable for induction or who is ordered to active duty as a member of a reserve component as a physician, or a dentist, or in an allied specialist category, shall be appointed, reappointed, or promoted to such grade or rank as may be commensurate with his professional education, experience, or ability provided that any person in a needed medical, dental, or allied specialist category who fails to qualify for, or who does not accept a commission, or whose commission has been terminated, may be used in his professional capacity in an enlisted grade.

8. Periods of active duty performed by such specialists in student programs prior to receipt of appropriate professional degree or in intern training shall not be counted toward establishing the qualification of such specialists for classification as a veteran exempt from liability for training and service.

9. It is the sense of Congress that the President provide for deferment of optometry students and premedical, preosteopathic, preveterinary, preoptometry, and predental students in numbers at least equal to the numbers of such male students now studying in colleges and universities.

10. Public Law 62, 85th Congress, amending the Universal Military Training and Service Act, as amended, to provide service liability for persons in medical, dental and allied specialist categories, expired July 1, 1959, and was reenacted by Public Law 86-4, 86th Congress, and expires July 1, 1963.

With the expiration of the requirement for special registration of medical, dental, and allied specialists, such specialists under the amendments of June 27, 1957, should notify their local boards within 10 days of the attainment of degrees in these fields.

ARMY, NAVY, AND AIR FORCE PROCUREMENT PROGRAMS

The following information summarizing the Army, Navy, and Air Force procurement programs has been submitted by the office of the Assistant Secretary of Defense (Health and Medical), current to June 26, 1958. It has been prepared so as to present a general portrayal of current procurement programs in the medical branches of the armed services insofar as they concern undergraduate and graduate medical education.

ARMY

Early Commissioning Program for Medical Students

Medical students may apply for commissions in the grade of second lieutenant, Medical Service Corps, Army Reserve, while attending medical school. Students participating in this program will be obligated to accept superseding appointments in the grade of first lieutenant, Medical Corps, Army Reserve, on graduation and, in accordance with the needs of the active Army, may be required to serve on active duty for a period of two years on completion of internship. Persons appointed under this program are assigned to Ready Reserve Units in appropriate medical corps vacancies in TOE and TD troop program units, USAR Schools, and USAR Control Groups (Annual Training).

Every effort will be made to place officers commissioned under this program on active duty on a date desired by them; however, no assurance can be given that they will be ordered to active duty at a particular time, since such action is contingent on programmed requirements of the active Army.

Participation in this program will not
increase the active service liability or o
the participant. However, participant
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Clinical Clerkship T

Participants in the Clinica
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hold appointments in the Medical Corps,
Reserve, as lieutenants, or will be commissio
in sufficient time to participate in the program. A limited number may also participate in the program as "student employees" under Civil Service. Students in Army Reserve status who are selected for this clinical clerkship must volunteer to perform not more than 60 days of active duty for training, including travel. Students who are assigned to a USAR Control Group (annual training) and are selected for the clerkship will fulfill their annual requirement for active Reserve participation by performing the above period of active duty for training. The students who are assigned to a TOE or TD Reserve Unit, or a USAR School will perform this training "in lieu of" the annual unit training (summer camp) requirement with their unit.

The program will consist of approximately eight weeks of instruction at Army teaching hospitals, which will be devoted to military medicine and other military instruction, and the remaining time will be divided into two equal periods, one embracing internal medicine and its subspecialties, the other surgery and its subspecialties. A preventive medicine program will also be available and will include one week of general orientation in military organizations, its functions and procedures, followed by detailed observation and assistance in a comprehensive preventive medicine program. Research clerkships are also available in a limited number for selected individuals at several medical facilities.

The program commences on July 1 each year and is of 45-60 days duration. A student selected for a clerkship between his sophomore-junior year is not eligible to apply for the clerkship between his junior-senior year.

Senior Medical Student Program

Selected senior medical students will be commissioned as second lieutenant, Medical Service Corps, Army Reserve, and will be permitted to continue their studies in their respective schools as officers on active duty with full pay and allowances until they complete their academic requirements for the degree of doctor of medicine, or until completion of the academic year in which enrolled at the time of entry on active duty, whichever occurs earlier. On completion of their medical

education, selected students will be required to accept appointments in the grade of first lieutenant, Medical Corps, Army Reserve; they must agree to participate in the National Intern Matching Program, Incorporated, and serve on active duty for three years immediately following their civilian or military internship. This includes time obligated under the Universal Military Training and Service Act, if applicable. Participants who are not matched for an Army internship will be released from active duty for one year to allow them to complete a civilian internship, and they will then be recalled to active duty for three years at the end of the 12-month period.

Military Intern Program

Selected graduates of approved medical schools will be commissioned as first lieutenants, Medical Corps, Army Reserve, and will be ordered to active duty for the purpose of completing a 12-month internship in a military hospital. Individuals participating in the program will not incur obligatory service; however, those individuals who will be liable for military service under the provision of any law will be required to serve that obligation immediately upon completion of their internships. Military interns will be encouraged to apply for Regular Army and residency training.

Applicants must agree to participate in the official co-operative plan of internship appointments for first-year internships as conducted by the National Intern Matching Program, Incorporated.

Military Resident Program

The Military Resident Training Program is established for the purpose of providing the number of specialists required to meet the needs of the Army for career Medical Corps officers. Residencies are sponsored in both military and civilian hospitals.

Officers of the Regular Army Medical Corps and individuals who meet the appointment criteria for the Regular Army are eligible to compete for residency training. Although appointment in the Regular Army is not a requirement for appointment as a resident, the purpose of the program is to provide the Army with sufficient career personnel having the required specialty training. Accordingly, applicants will be considered on the following priority basis: (1) Regular Army Medical Corps officers, (2) Reserve Medical Corps officers on active duty, including interns who are concurrently applying for Regular Army appointment, (3) civilian physicians, including interns, who apply for Regular Army appointment, and (4) all other applicants.

Inasmuch as the number of applications received for participation in the Army residency program far exceeds the number of appointments available, consideration should be given to seeking a Regular Army commission in order to establish a priority for consideration for the residency program. Appointment for the program ordinarily will not b made more than one year in advance, and applications for Regular Army in connection with residency training will not be considered for appointment in a grade higher than captain. Individuals selected for training who have not completed the appropriate Army Medical Service orientation course, or an equivalent period of active duty as a medical officer, as determined by the surgeon general in each case, will be required to undergo such training prior to entering residencies. Selections will be made in November of each year. Appointments to fill remaining vacancies will be made from applications as received.

Individuals placed in residencies in Army hospitals will be required to serve one year on a duty status for each year of training received.

In the event training is not available in Army hospitals on the next starting date after approval of an application in a specialty that is critical to the needs of the Army, an opportunity will be offered to applicants approved for Regular Army to obtain such training in a civilian hospital approved by the Council on Medical Education and Hospitals of the American Medical Association. Individuals participating in the program in civilian hospitals under this policy are required to serve on active duty for two years for the first year of training received and one year for each subsequent year.

NAVY

The Ensign 1915 USNR Program

After passage of the Selective Service Act of 1940, many medical students who were obligated for military service by the Act indicated their desire to affiliate with the Naval Reserve in order to assure that their period of active duty would be with the Navy's Medical Department. To make this possible and to provide deferment from active duty until graduation, the Ensign, Probationary (Medical) Program was established before the onset of World War II. The first appointments late in 1941 were limited to third-year and fourth-year medical students attending class "A" (approved) medical schools. Within a few months, however, the program was expanded to include first-year and second-year medical students, and it has since come to be known as the Ensign 1915 Program.

The qualifications for appointment as Ensign, 1915, are as follows:

A. Sex: Men and Women

B. Age

(1) Candidates with no prior military service should be at least 19 and of such age that upon expected date of graduation, they will be under 33. The maximum age limit with prior active military service may be adjusted on a month-to-month basis, depending upon the number of months of active military service performed, but in no case to exceed 36 months. Applications cannot be accepted y person who will have passed his or

8. Periods of active duty performed by such specialists in student programs prior to receipt of appropriate professional degree or in intern training shall not be counted toward establishing the qualification of such specialists for classification as a veteran exempt from liability for training and service.

9. It is the sense of Congress that the President provide for deferment of optometry students and premedical, preosteopathic, preveterinary, preoptometry, and predental students in numbers at least equal to the numbers of such male students now studying in colleges and universities.

10. Public Law 62, 85th Congress, amending the Universal Military Training and Service Act, as amended, to provide service liability for persons in medical, dental and allied specialist categories, expired July 1, 1959, and was reenacted by Public Law 86-4, 86th Congress, and expires July 1, 1963.

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Every effort will be made to place officers commissioned under this program on active duty on a date desired by them; however, no assurance can be given that they will be ordered to active duty at a particular time, since such action is contingent on programmed requirements of the active Army. Participation in this program will not in itself increase the active service liability or obligation of the participant. However, participants will be required to certify to their understanding that appointment prior to attaining age 26 incurs an obligation for active participation in the Reserve training unless excused under regulations prescribed by the Secretary of the Army.

Clinical Clerkship Training Program

Participants in the Clinical Clerkship Training Program will be medical students at the sophomore-junior and/or junior-senior level, who now hold appointments in the Medical Corps, Army Reserve, as lieutenants, or will be commissioned in sufficient time to participate in the program. A limited number may also participate in the program as "student employees" under Civil Service. Students in Army Reserve status who are selected for this clinical clerkship must volunteer to perform not more than 60 days of active duty for training, including travel. Students who are assigned to a USAR Control Group (annual training) and are selected for the clerkship will fulfill their annual requirement for active Reserve participation by performing the above period of active duty for training. The students who are assigned to a TOE or TD Reserve Unit, or a USAR School will perform this training "in lieu of" the annual unit training (summer camp) requirement with their unit.

The program will consist of approximately eight weeks of instruction at Army teaching hospitals, which will be devoted to military medicine and other military instruction, and the remaining time will be divided into two equal periods, one embracing internal medicine and its subspecialties, the other surgery and its subspecialties. A preventive medicine program will also be available and will include one week of general orientation in military organizations, its functions and procedures, followed by detailed observation and assistance in a comprehensive preventive medicine program. Research clerkships are also available in a limited number for selected individuals at several medical facilities.

The program commences on July 1 each year and is of 45-60 days duration. A student selected for a clerkship between his sophomore-junior year is not eligible to apply for the clerkship between his junior-senior year.

Senior Medical Student Program

Selected senior medical students will be commissioned as second lieutenant, Medical Service Corps, Army Reserve, and will be permitted to continue their studies in their respective schools as officers on active duty with full pay and allowances until they complete their academic requirements for the degree of doctor of medicine, or until completion of the academic year in which enrolled at the time of entry on active duty, whichever occurs earlier. On completion of their medical

education, selected students will be required to accept appointments in the grade of first lieutenant, Medical Corps, Army Reserve; they must agree to participate in the National Intern Matching Program, Incorporated, and serve on active duty for three years immediately following their civilian or military internship. This includes time obligated under the Universal Military Training and Service Act, if applicable. Participants who are not matched for an Army internship will be released from active duty for one year to allow them to complete a civilian internship, and they will then be recalled to active duty for three years at the end of the 12-month period.

Military Intern Program

Selected graduates of approved medical schools will be commissioned as first lieutenants, Medical Corps, Army Reserve, and will be ordered to active duty for the purpose of completing a 12-month internship in a military hospital. Individuals participating in the program will not incur obligatory service; however, those individuals who will be liable for military service under the provision of any law will be required to serve that obligation immediately upon completion of their internships. Military interns will be encouraged to apply for Regular Army and residency training.

Applicants must agree to participate in the official co-operative plan of internship appointments for first-year internships as conducted by the National Intern Matching Program, Incorporated.

Military Resident Program

The Military Resident Training Program is established for the purpose of providing the number of specialists required to meet the needs of the Army for career Medical Corps officers. Residencies are sponsored in both military and civilian hospitals.

Officers of the Regular Army Medical Corps and individuals who meet the appointment criteria for the Regular Army are eligible to compete for residency training. Although appointment in the Regular Army is not a requirement for appointment as a resident, the purpose of the program is to provide the Army with sufficient career personnel having the required specialty training. Accordingly, applicants will be considered on the following priority basis: (1) Regular Army Medical Corps officers, (2) Reserve Medical Corps officers on active duty, including interns who are concurrently applying for Regular Army appointment, (3) civilian physicians, including interns, who apply for Regular Army appointment, and (4) all other applicants.

Inasmuch as the number of applications received for participation in the Army residency program far exceeds the number of appointments available, consideration should be given to seeking a Regular Army commission in order to establish a priority for consideration for the residency program. Appointment for the program ordinarily will not be made more than one year in advance, and applications for Regular Army in connection with residency training will not be considered for appointment in a grade higher than captain. Individuals selected for training who have not completed the appropriate Army Medical Service orientation course, or an equivalent period of active duty as a medical officer, as determined by the surgeon general in each case, will be required to undergo such training prior to entering residencies. Selections will be made in November of each year. Appointments to fill remaining vacancies will be made from applications as received.

Individuals placed in residencies in Army hospitals will be required to serve one year on a duty status for each year of training received.

In the event training is not available in Army hospitals on the next starting date after approval of an application in a specialty that is critical to the needs of the Army, an opportunity will be offered to applicants approved for Regular Army to obtain such training in a civilian hospital approved by the Council on Medical Education and Hospitals of the American Medical Association. Individuals participating in the program in civilian hospitals under this policy are required to serve on active duty for two years for the first year of training received and one year for each subsequent year.

NAVY

The Ensign 1915 USNR Program

After passage of the Selective Service Act of 1940, many medical students who were obligated for military service by the Act indicated their desire to affiliate with the Naval Reserve in order to assure that their period of active duty would be with the Navy's Medical Department. To make this possible and to provide deferment from active duty until graduation, the Ensign, Probationary (Medical) Program was established before the onset of World War II. The first appointments late in 1941 were limited to third-year and fourth-year medical students attending class "A" (approved) medical schools. Within a few months, however, the program was expanded to include first-year and second-year medical students, and it has since come to be known as the Ensign 1915 Program.

The qualifications for appointment as Ensign, 1915, are as follows:

A. Sex: Men and Women

B. Age

(1) Candidates with no prior military service should be at least 19 and of such age that upon expected date of graduation, they will be under 33. The maximum age limit with prior active military service may be adjusted on a month-to-month basis, depending upon the number of months of active military service performed, but in no case to exceed 36 months. Applications cannot be accepted from any person who will have passed his or her 36th

8. Periods of active duty performed by such specialists in student programs prior to receipt of appropriate professional degree or in intern training shall not be counted toward establishing the qualification of such specialists for classification as a veteran exempt from liability for training and service.

9. It is the sense of Congress that the President provide for deferment of optometry students and premedical, preosteopathic, preveterinary, preoptometry, and predental students in numbers at least equal to the numbers of such male students now studying in colleges and universities.

10. Public Law 62, 85th Congress, amending the Universal Military Training and Service Act, as amended, to provide service liability for persons in medical, dental and allied specialist categories, expired July 1, 1959, and was reenacted by Public Law 86-4, 86th Congress, and expires July 1, 1963.

With the expiration of the requirement for special registration of medical, dental, and allied specialists, such specialists under the amendments of June 27, 1957, should notify their local boards within 10 days of the attainment of degrees in these fields.

ARMY, NAVY, AND AIR FORCE PROCUREMENT PROGRAMS

The following information summarizing the Army, Navy, and Air Force procurement programs has been submitted by the office of the Assistant Secretary of Defense (Health and Medical), current to June 26, 1958. It has been prepared so as to present a general portrayal of current procurement programs in the medical branches of the armed services insofar as they concern undergraduate and graduate medical education.

ARMY

Early Commissioning Program for Medical Students

Medical students may apply for commissions in the grade of second lieutenant, Medical Service Corps, Army Reserve, while attending medical school. Students participating in this program will be obligated to accept superseding appointments in the grade of first lieutenant, Medical Corps, Army Reserve, on graduation and, in accordance with the needs of the active Army, may be required to serve on active duty for a period of two years on completion of internship. Persons appointed under this program are assigned to Ready Reserve Units in appropriate medical corps vacancies in TOE and TD troop program units, USAR Schools, and USAR Control Groups (Annual Training).

Every effort will be made to place officers commissioned under this program on active duty on a date desired by them; however, no assurance can be given that they will be ordered to active duty at a particular time, since such action is contingent on programmed requirements of the active Army.

Participation in this program will not in itself increase the active service liability or obligation of the participant. However, participants will be required to certify to their understanding that appointment prior to attaining age 26 incurs an obligation for active participation in the Reserve training unless excused under regulations prescribed by the Secretary of the Army.

Clinical Clerkship Training Program

Participants in the Clinical Clerkship Training Program will be medical students at the sophomore-junior and/or junior-senior level, who now hold appointments in the Medical Corps, Army Reserve, as lieutenants, or will be commissioned in sufficient time to participate in the program. A limited number may also participate in the program as "student employees" under Civil Service. Students in Army Reserve status who are selected for this clinical clerkship must volunteer to perform not more than 60 days of active duty for training, including travel. Students who are assigned to a USAR Control Group (annual training) and are selected for the clerkship will fulfill their annual requirement for active Reserve participation by performing the above period of active duty for training. The students who are assigned to a TOE or TD Reserve Unit, or a USAR School will perform this training "in lieu of" the annual unit training (summer camp) requirement with their unit.

The program will consist of approximately eight weeks of instruction at Army teaching hospitals, which will be devoted to military medicine and other military instruction, and the remaining time will be divided into two equal periods, one embracing internal medicine and its subspecialties, the other surgery and its subspecialties. A preventive medicine program will also be available and will include one week of general orientation in military organizations, its functions and procedures, followed by detailed observation and assistance in a comprehensive preventive medicine program. Research clerkships are also available in a limited number for selected individuals at several medical facilities.

The program commences on July 1 each year and is of 45-60 days duration. A student selected for a clerkship between his sophomore-junior year is not eligible to apply for the clerkship between his junior-senior year.

Senior Medical Student Program

Selected senior medical students will be commissioned as second lieutenant, Medical Service Corps, Army Reserve, and will be permitted to continue their studies in their respective schools as officers on active duty with full pay and allowances until they complete their academic requirements for the degree of doctor of medicine, or until completion of the academic year in which enrolled at the time of entry on active duty, whichever occurs earlier. On completion of their medical

education, selected students will be required to accept appointments in the grade of first lieutenant, Medical Corps, Army Reserve; they must agree to participate in the National Intern Matching Program, Incorporated, and serve on active duty for three years immediately following their civilian or military internship. This includes time obligated under the Universal Military Training and Service Act, if applicable. Participants who are not matched for an Army internship will be released from active duty for one year to allow them to complete a civilian internship, and they will then be recalled to active duty for three years at the end of the 12-month period.

Military Intern Program

Selected graduates of approved medical schools will be cmmissioned as first lieutenants, Medical Corps, Army Reserve, and will be ordered to active duty for the purpose of completing a 12-month internship in a military hospital. Individuals participating in the program will not incur obligatory service; however, those individuals who will be liable for military service under the provision of any law will be required to serve that obligation immediately upon completion of their internships. Military interns will be encouraged to apply for Regular Army and residency training.

Applicants must agree to participate in the official co-operative plan of internship appointments for first-year internships as conducted by the National Intern Matching Program, Incorporated.

Military Resident Program

The Military Resident Training Program is established for the purpose of providing the number of specialists required to meet the needs of the Army for career Medical Corps officers. Residencies are sponsored in both military and civilian hospitals.

Officers of the Regular Army Medical Corps and individuals who meet the appointment criteria for the Regular Army are eligible to compete for residency training. Although appointment in the Regular Army is not a requirement for appointment as a resident, the purpose of the program is to provide the Army with sufficient career personnel having the required specialty training. Accordingly, applicants will be considered on the following priority basis: (1) Regular Army Medical Corps officers, (2) Reserve Medical Corps officers on active duty, including interns who are concurrently applying for Regular Army appointment, (3) civilian physicians, including interns, who apply for Regular Army appointment, and (4) all other applicants.

Inasmuch as the number of applications received for participation in the Army residency program far exceeds the number of appointments available, consideration should be given to seeking a Regular Army commission in order to establish a priority for consideration for the residency program. Appointment for the program ordinarily will not be made more than one year in advance, and applications for Regular Army in connection with residency training will not be considered for appointment in a grade higher than captain. Individuals selected for training who have not completed the appropriate Army Medical Service orientation course, or an equivalent period of active duty as a medical officer, as determined by the surgeon general in each case, will be required to undergo such training prior to entering residencies. Selections will be made in November of each year. Appointments to fill remaining vacancies will be made from applications as received.

Individuals placed in residencies in Army hospitals will be required to serve one year on a duty status for each year of training received.

In the event training is not available in Army hospitals on the next starting date after approval of an application in a specialty that is critical to the needs of the Army, an opportunity will be offered to applicants approved for Regular Army to obtain such training in a civilian hospital approved by the Council on Medical Education and Hospitals of the American Medical Association. Individuals participating in the program in civilian hospitals under this policy are required to serve on active duty for two years for the first year of training received and one year for each subsequent year.

NAVY

The Ensign 1915 USNR Program

After passage of the Selective Service Act of 1940, many medical students who were obligated for military service by the Act indicated their desire to affiliate with the Naval Reserve in order to assure that their period of active duty would be with the Navy's Medical Department. To make this possible and to provide deferment from active duty until graduation, the Ensign, Probationary (Medical) Program was established before the onset of World War II. The first appointments late in 1941 were limited to third-year and fourth-year medical students attending class "A" (approved) medical schools. Within a few months, however, the program was expanded to include first-year and second-year medical students, and it has since come to be known as the Ensign 1915 Program.

The qualifications for appointment as Ensign, 1915, are as follows:

A. Sex: Men and Women

B. Age

(1) Candidates with no prior military service should be at least 19 and of such age that upon expected date of graduation, they will be under 33. The maximum age limit with prior active military service may be adjusted on a month-to-month basis, depending upon the number of months of active military service performed, but in no case to exceed 36 months. Applications cannot be accepted from any person who will have passed his or her 36th

birthday when he or she becomes eligible for superseding appointment in the Medical Corps, U. S. Naval Reserve following graduation from medical school.

C. Educational

(1) Should be within 120 days of completion of all academic work required for enrollment in medical school.

(2) Should be in attendance or have been accepted for and be within six months or less of the date of the next entering class at one of the American or certain of the Canadian medical schools accredited by the Council on Medical Education and Hospitals of the American Medical Association, including approved schools of the basic medical sciences in the United States and Canada. Applications cannot be accepted from students who will attend a medical school in a foreign country other than Canada.

(3) Should NOT have commenced the final year of medical school.

D. Professional

(1) Applicants are required to establish professional fitness and aptitude for the Naval Service through interviews and a review of college and employment records.

E. Physical Standards

(1) Should be found physically qualified for appointment to commissioned status in accordance with established regulations.

The primary objectives of this program are to provide (1) an opportunity for qualified medical students to affiliate with the Naval Reserve as commissioned officers while still in medical school; (2) assurance that these officers will be able to complete their medical studies and internship prior to fulfilling their obligation for active military duty; (3) assurance that, when they do enter the service, it will be within the Navy's Medical Department; and (4) a primary source of qualified candidates for the Naval Intern Program and for the Medical Corps of the Navy and Naval Reserve.

As an added incentive for membership in the Ensign 1915 Program, there has been established a 30-60 day active duty research clerkship training program at naval research activities throughout the United States. This program provides orientation and indoctrination into medical research as well as on-the-job training for the undergraduate medical student during his vacation from medical school. Full pay and allowances are authorized for these selected officers while so serving on active duty. Medical students who are commissioned as Ensign, 1915 USNR, and who have successfully completed the first year of medical school are eligible to participate in this program. Research clerkships offer a detailed review of the specific research program being conducted at the training activity. A part of the training is spent in each research department, and the trainee serves as an assistant in actual laboratory research on a specific project under way at that time.

Also established are clinical clerkships at Naval teaching hospitals throughout the United States. Beginning July 1 of each year, this program offers quotas for selected medical students who have completed the second year of medical school, 30 to 60 days of active duty for training during vacation from medical school. Clinical clerkships are planned to provide indoctrination and orientation into naval medicine, rotation through the major professional services of a naval teaching hospital, and performance of on-the-job training duties commensurate with the individual's professional attainments.

Normally each year during the summer months a limited number of mature medical students holding commission as Ensign, 1915, are authorized to participate in NROTC-Midshipmen Cruises. Selections for this important training are made from students who have completed at least their second year of medical school with priority being given those who have completed their third year. Trainees receive an excellent indoctrination and orientation into the practices of naval medicine aboard ship under the supervision of experienced medical officers of the Regular Navy and Naval Reserve.

To assist the medical student financially, and to attract future doctors of medicine toward a career in the Navy Medical Corps, the Senior Medical Student Program was authorized by the Secretary of the Navy. To be eligible for participation, the individual student must be an Ensign, 1915 USNR, or agree to accept such an appointment if selected. Further, he must have completed his third year of medical school and be eligible for enrollment in the ensuing year. During attendance in medical school, these officers serve on active duty, receiving the full pay and allowances of their rank. In return for participation in this program, the individual serves one year plus the 24 months obligated by the Universal Military Training and Service Act, as amended.

Here are some important facts concerning the Senior Medical Student Program:

(1) This program is open to qualified students enrolled at medical schools accredited by the Council on Medical Education and Hospitals of the American Medical Association. Students who have completed their second year of medical school may make application for this training at an Office of Naval Officer Procurement. Active duty commences and continues while in attendance during their senior academic year. To be eligible for participation, he must be an Ensign, 1915 U. S. Naval Reserve, or agree to accept such an appointment if selected. A board convened in the Bureau of Medicine and Surgery selects the candidates for participation in this program.

(2) Physical standards of this program are the same as those established for Regular Navy staff corps officers.

(3) Active duty orders are mailed to the student via the Professor of Naval Science or the District

Commandant. Active duty commences upon receipt of such orders and completion of proper reporting endorsements.

(4) The student agrees, in writing, to accept a Regular Navy commission, and if a Regular Navy commission is not tendered, to accept an appointment in the Naval Reserve.

(5) In accepting an appointment in the Regular Navy or Naval Reserve, as a result of having active service in the Senior Medical Student Program as an Ensign, 1915, he is obligated to serve on active duty and to retain the commission for a period of three years. This active service will commence upon completion of not more than 12 months of a civilian or Naval Internship. Providing that the student has 24 months obligated military service to perform, this active duty affords a splendid opportunity to discharge the military obligation and serve an additional year in return for the benefits received in the Senior Medical Student Program. With no obligated military service to perform, upon enrollment in the Senior Medical Student Program, the student obligates himself to serve for the same period of three years.

(6) As a medical student, he receives the full pay allowances of an Ensign, 1915, while so enrolled on active duty. Pay and allowances are based on longevity as follows:

(*a*) Less than two years and no dependents, he receives $338.58 per month; with dependents (a member of his family or household dependent upon him for financial support) he receives $355.68 per month.

(*b*) Over two but less than three years and no dependents, he receives $366.28 per month; with dependents, he receives $384.38 per month.

(*c*) Over three and no dependents, he receives $429.28 per month; with dependents he receives $447.38 per month.

(7) In addition to the pay and allowances, the student is credited with 2½ days of annual leave for each 30 days of active duty served.

(8) The wearing of the Naval uniform is permitted only when authorized by appropriate naval authority.

(9) Timing is very important. An average of four months is required to completely process each application. Feb. 1 each year is the absolute deadline that completed applications must be forwarded to the Bureau of Naval Personnel, Navy Department, Washington, D. C. This is necessary so that sufficient time is given to the board in the Bureau of Medicine and Surgery to pass on the professional qualifications and the board in the Bureau of Naval Personnel to pass on the over-all qualifications of each applicant. Those selected are required to meet the moral, mental, and physical standards of Navy acceptance. All applicants will be notified by individual letter of their acceptance or rejection not later than the first week in May.

Naval Internships

Naval internships are 12 months in duration, are rotating in type, and conform in all respects with the requirements of the Council on Medical Education and Hospitals of the American Medical Association. These compare most favorably with the best civilian internships, and each year the number of applicants considerably exceeds the number of available naval internships. Internships are offered at the U. S. Naval Hospitals located at Camp Pendleton, Calif.; Oakland, Calif.; San Diego, Calif.; Jacksonville, Fla.; Pensacola, Fla.; Great Lakes, Ill.; Bethesda, Md.; Chelsea, Mass.; St. Albans, N. Y.; Philadelphia; Newport, R. I.; Charleston, S. C.; Portsmouth, Va.; and Bremerton, Wash.

All naval interns are selected and matched to the Navy by the National Intern Matching Program, Incorporated. It is not necessary for the medical student to be a participant in the Ensign 1915 USNR Program in order to apply and be accepted for a naval internship. On the other hand, if the Ensign 1915 USNR candidate does not desire a naval internship, he should list only the civilian hospitals in the order of his preference, and in this way he will not be competing with those who desire a naval internship and who request to be so matched. The Ensign 1915 candidate who is matched to a civilian internship will be placed on inactive duty during the period of his internship, following completion of which he will be called to active duty in compliance with his previous service agreement.

The basic requirements for a naval internship include the following: (1) be a graduate or potential graduate of a medical school approved by the American Medical Association; (2) be a citizen of the United States; (3) be registered with and his name appear in the Official Directory of Students published by the National Intern Matching Program, Inc.; and (4) meet the prescribed physical standards for a commission in the U. S. Naval Reserve.

In order to become eligible for consideration for a naval internship, candidates must first make application for a commission in the Naval Medical Corps. This can be accomplished by visiting or writing to the nearest Office of Naval Officer Procurement or the nearest U. S. Naval Hospital in the continental United States. In applying for a naval internship it is recommended that five (5) naval hospitals be listed in the order of preference. Generally assignments are made from among the first three listed. The candidate applies, as far as the matching is concerned, directly to the Navy and not to the specific hospital. If matched to the Navy, every effort is made to place the candidate in his first choice, but if this is not possible, he will be assigned to another hospital of his choice. In the matching program the student is matched to the service and not to a particular hospital within it.

Applications for commission in the Naval Medical Corps for intern training are accepted between Sept. 1 and Dec. 1 each year. That portion of the application pertaining to internship is accepted between Oct. 1 and Dec. 1. Early submission of applications is strongly recommended.

Any additional information may be obtained from the Chief, Bureau of Medicine and Surgery, Department of the Navy, Washington 25, D. C.

Naval Residency Training Programs

Eight U. S. naval hospitals are now approved for residency training in the various clinical specialties of medicine and surgery by the Council on Medical Education and Hospitals of the American Medical Association and by the respective American Specialty Boards. These naval hospitals are located at Chelsea, Mass.; St. Albans, N. Y.; Philadelphia; Bethesda, Md.; Portsmouth, Va.; Great Lakes, Ill.; Oakland, Calif.; and San Diego, Calif. Residency training for medical officers is also actively sponsored by the U. S. Navy in selected outstanding civilian hospitals, schools, and medical centers of the United States in those few specialties wherein the Navy does not operate formalized training programs. U. S. Naval Hospital residency training activities embrace the specialties of anesthesiology, cardiovascular disease, dermatology and syphilology, general practice, internal medicine, neurology, obstetrics and gynecology, ophthalmology, orthopedic surgery, otolaryngology, pathology, pediatrics, psychiatry, radiology, surgery, thoracic surgery, and urology. Formally approved training in civilian institutions is conducted in allergy, plastic surgery, neurological surgery, preventive medicine and public health, and in children's orthopedic surgery.

Medical officers eligible for assignment to duty as a resident are Regular Navy officers and those Reserve medical officers who are willing to accept and can qualify for a commission in the Regular Navy. Requests for residency training duty should be forwarded to the Chief of the Bureau of Medicine and Surgery, Navy Department, Washington 25, D. C. All such requests are acted upon by the Bureau Advisory Board on professional training matters. This board makes recommendations in accordance with the merits of each case, taking into consideration the professional experience, background, and aptitude of the candidate and the needs of the service in the particular specialty in which training is desired. One year of obligated service is required for each year of training received in a Naval hospital. Two years of obligated service are required for the first year of training received in civilian institutions and one year of obligated service for each successive year so spent.

It is the policy of the Bureau of Medicine and Surgery to continue a resident in training until formal requirements, leading to eligibility to undergo examination by an American Specialty Board, have been met. This procedure will be strictly adhered to in every case where the needs of the service permit, barring national emergencies, provided that such an arrangement remains mutually agreeable and satisfactory aptitude and progress as a resident are demonstrated. The highest priority in the assignment of naval medical officers to residency training is given those who have completed or are about to complete a normal tour of active duty with an operational unit of the U. S. Navy at sea or on foreign shore stations.

Other Graduate Training for Naval Medical Officers, Including the Military Medical Specialties

Aviation Medicine.—The School of Aviation Medicine at Pensacola, Fla., convenes three classes annually of approximately 40 students, for didactic instruction in aviation medicine and actual instruction in flight and ground school. Each class is of about six months duration. On completion of this course of instruction they are designated naval flight surgeons and assigned to a two-year period of operational duty. Additionally, the School of Aviation Medicine is approved for residency training in aviation medicine. This training may be requested after completion of the two-year operational duty assignment and consists of one year of public health at a civilian institution and two years of residency training in aviation medicine at the school in Pensacola or any of the approved aviation research laboratories. They are then considered board eligible for certification in aviation medicine after another two-year operational tour. Further opportunities are available in several large naval laboratories for work in research related to aviation medicine. The laboratories are located at Johnsville, Pa.; Philadelphia; the School of Aviation Medicine, Pensacola, Fla.; and the Naval Medical Research Institute, National Naval Medical Center, Bethesda, Md. A medical officer interested in the aeronautical aspects would do well to consider this advanced training.

Submarine Medicine.—This military medical specialty supports all phases of underwater operations in the Navy. Training in this specialty is particularly applicable to those having an interest in occupational medicine, public health, radiobiology, or research. The basic six months' course of training includes lectures, demonstrations, laboratory work, practical experience, and cruises in submarines, rescue vessels, and tenders as available. The major part of the course is given at the Submarine School and Medical Research Laboratory at the Submarine Base, New London, Connecticut.

On completion of the first four months, two alternatives are available to the student. During the last eight weeks he may elect to either take a course in radiobiology or underwater physiology.

The course in radiobiology is taught at the Nuclear-Power Division of the Submarine School. The subject matter embraces the essentials of nuclear physics, nucle[illegible]lth physics, and the biological [illegible]. Medical officers who complete this course will be assigned to duty with the Nuclear Power Submarine Program.

The course in underwater physiology is taught at the U. S. Naval Deep Sea Diving School, Naval Weapons Plant, Washington, D. C. Here the student learns about the physiological problems involved in diving and underwater swimming. He also learns about diving by completing deep sea diving exercises. The course also covers the recognition and treatment of pathological conditions resulting from exposure to high atmospheric pressures. Those completing this course will be assigned duties with conventional submarine squadrons or operational units employing divers and underwater swimmers.

Career medical officers will be provided with an opportunity for cross-training at a later date. That is, they may complete the course, radiobiology or underwater physiology, they did not elect in the basic training program.

On completion of a tour of duty with an operational unit the medical officer may apply for postgraduate training in various fields. He may prepare for certification in preventive medicine by attending one of the public health schools and subsequent field duty ashore and afloat. He may prepare himself for a career in research by a postgraduate year at the University of Pennsylvania College of Medicine followed by duty at naval laboratories and with operational units. Clinical medical specialty training in all fields is available and having served with an operational unit adds weight to one's application.

Research Program.—The Navy offers medical officer billets for military medical research careers. These opportunities embrace basic medical research in aviation medicine, submarine medicine, clinical specialties, amphibious and field medicine, tropical and exotic diseases, and in the areas of the medical problems of nuclear, biological, and chemical warfare defense. These billets are distributed among 15 in-service laboratories, strategically located throughout the world, and represent the program indicated above.

Amphibious and Marine Corps Field Medicine.—Recognized as an important military operational medical specialty, this training is conducted at Camp Lejeune, N. C., Camp Pendleton, Calif., and the Marine Corps Educational Center, Senior School, Quantico, Va. This specialty offers valuable training in the methods of sorting (triage), management, and evacuation of mass casualties, research and development of field medical equipment, field sanitation methodology and practices, medical logistic support, large scale medical planning, and efficient patient care in field combat.

Nuclear Medicine.—Graduate courses for medical officers are conducted at several U. S. Naval Hospitals, in affiliation with civilian institutions. Additional graduate courses in radiobiology are sponsored by the Navy for medical officers at Reed College, Portland, Ore., and the University of Rochester, Rochester, N. Y., to meet present and future needs of the Navy for personnel trained in the fields of nuclear propulsion, radiological safety and special weapons effects. Formal long courses for radiology and other residents are conducted in the clinical use of radioisotopes at the U. S. Naval Medical School, National Naval Medical Center, Bethesda, Md. This latter course is approved by the Atomic Energy Commission and is designed to fulfill the needs of those who wish to appear for future examination for certification by the American Board of Radiology, as well as those residents in other specialties who may need to acquire a better understanding of the clinical utilization of radioisotopes in diagnostic and therapeutic procedures.

AIR FORCE

The Air Force presently conducts the Senior Medical Student Program, as well as Sponsored Internships and Residencies in military and civilian hospitals. Applicants must be United States citizens, be morally, physically and educationally qualified, and must not be nor have been conscientious objectors. Complete details on any of the following programs may be obtained by writing to the Surgeon General, United States Air Force, Washington 25, D. C.

The Senior Medical Student Program

The Air Force Senior Medical Student Program is available to Junior Medical Students. The application period for this program is Nov. 1 to March 1 of the student's junior year. Those selected are commissioned as Second Lieutenants and are called to active duty about Sept. 15. Selected applicants agree to accept reappointment as First Lieutenants on graduation and to apply for a sponsored internship, either military or civilian. Those not selected for sponsored intern training are released from active duty for one year to intern under private contract. Selected applicants incur a three-year obligation, which must be served immediately upon completion of internship. No additional obligated service is incurred through the combination of the student program and either of the intern programs. Tuition, books, and other related expenses must be paid for by the student.

Air Force Sponsored Military and Civilian Internships

The Air Force Intern Training Program, begun in 1950, is designed as a Regular Officer Procurement Program. To be considered, applicants must meet general eligibility requirements stated above, must not be more than 32 years of age, and must be graduates of medical schools acceptable to the Surgeon General. Selections are made on the basis of scholastic standing, physical fitness, and military aptitude and inclination.

Military Internships

For the year beginning July 1, 1960, the Air Force will sponsor ninety-two (92) interns in military hospitals, selected through the National Intern Matching Program. Interested students must submit their applications to the Surgeon General, United States Air Force, not later than Dec. 1, 1959. Selectees are appointed First Lieutenants, Reserve of the Air Force (Medical Corps), and agree to serve on active duty for three years including the year of internship. This concurrently satisfies the individual's obligation under the Universal Military Training and Service Act. In applying for an Air Force internship, it is recommended that five Air Force hospitals be listed in the order of preference. Generally assignments are made from among the first three listed. Internships are of one year duration and are of the general rotating type. Training is directed by military and civilian physicians and includes a wide range of clinical material, using modern medical, surgical, and radiological facilities. It fully satisfies the requirements of the Council on Medical Education and Hospitals of the American Medical Association.

Civilian Internships

For the year beginning July 1, 1960, the Air Force will sponsor approximately 80 interns in approved civilian hospitals. The application period for internships commences on July 1, closes on April 1 of each year. Applicants for off-term internships should apply approximately six months prior to the starting date of the training. Selected applicants serve on active duty as First Lieutenants, Reserve of the Air Force (Medical Corps), and must agree to serve for a total of four years, including the year of internship. This concurrently satisfies the individual's obligation under the Universal Military Training and Service Act.

Residency Training Program

This program is designed to provide competent, well-trained career officer specialists for responsible positions in Air Force medical facilities. Participation is normally limited to members of the Regular Air Force with outstanding qualifications who are genuinely motivated for careers in the Air Force. Physicians accepted for the program are trained in Air Force, Army, and civilian hospitals (including nonmilitary Government hospitals). For the year beginning July 1, 1960, the program provides for a maximum of 375 residents, about equally divided between military and civilian hospitals. Approximately 120 first-year residency spaces are available; 40 in Air Force hospitals, 30 in Army hospitals, and 50 in civilian hospitals.

Training is available in the recognized medical specialties according to the needs of the Air Force. Competition is keen since many more applications are usually received than may be approved. The chances of an applicant for acceptance are naturally better if he desires training in a specialty in demand. The Air Force needs specialists in psychiatry, neurology, general practice, otolaryngology, radiology, gastroenterology, and infectious diseases.

The USAF Hospital Lackland, Lackland Air Force Base, San Antonio, Texas, a new teaching hospital of the Air Force, offers approved residency training in anesthesiology, general surgery, internal medicine, obstetrics and gynecology, ophthalmology, orthopedic surgery, pathology, pediatrics, radiology, and urology. These programs normally commence on July 1.

Physicians who enter this program are expected to remain in training until they have completed the minimum formal training requirements of the specialty boards, provided that progress is satisfactory. Applications for a Regular Air Force commission and residency training may be initiated simultaneously and at any time following the beginning of the internship. The Air Force Medical Service prefers to select residents from among those highly qualified physicians who have had an opportunity to observe the practice of medicine in the Air Force. A period of active duty permits the individual to evaluate the service from a career viewpoint. It also affords the Air Force an opportunity to evaluate the performance of the individual in terms of his suitability and adaptability for a career in Air Force medicine.

Normally, approximately six or more months are required to process the applications for a Regular Air Force commission and residency training. It is recommended, however, that the applications be submitted in August or September for training to begin between the following July and January. Such applications must reach Headquarters United States Air Force not later than Nov. 15.

The USAF Aviation Medicine Specialty Training Program leading to board certification in Aviation Medicine is a comprehensive program of five years' duration. Applicants must be graduates of the Primary Course of Aviation Medicine and have had a minimum of nine months practice as an Aviation Medical Examiner. Applicants must be officers of the Regular Air Force, physically and professionally qualified, and be no more than 34 years of age when the class convenes. Applications must arrive at Headquarters United States Air Force not later than Jan. 1 for entrance into program beginning the following September.

Further information pertaining to the program, including the application procedures, may be obtained from the Chief, Medical Education Division, Office of the Surgeon General, USAF, Washington 25, D. C.

UNDERGRADUATE AND GRADUATE MEDICAL TRAINING PROGRAMS IN THE VETERANS ADMINISTRATION

The following material reviewing the Undergraduate and Graduate Medical Training Programs in the Veterans Administration has been submitted by the Director, Education Service, Department of Medicine and Surgery of the Veterans Administration.

The Veterans Administration–Medical School relationship continues to provide the basic medium for undergraduate and graduate medical training in VA hospitals. Confidence in the principles of this association and acceptability of the current working relationships has been strongly reaffirmed by a letter survey of opinions from all VA hospital managers and deans of associated medical schools. The results of this survey were published in the *Journal of Medical Education*.[20]

As of May 30, 1959, there were 2,669 physician residents on duty, of whom 265 were in career status. Those in the latter group receive the pay of full-time physicians in return for a specified period of assigned service at the conclusion of their residency training. The career residents were distributed in six specialty groups as shown in table 48.

Due to a temporary suspension of reporting in 1959, exact data are not available for the distribution of noncareer residents by specialty or for the number and administrative type of programs in operation during this year. We will resume the reporting of these data in the next year.

Table 48.—*Veterans Administration Career Residents, May, 1959*

Anesthesiology	23
Neurology	12
Pathology	24
Physical Medicine	25
Psychiatry	157
Radiology	24
Total	265

The assignment of medical students to Veterans Administration hospitals for clinical clerkship training has continued at a level approximating that for the previous academic year. A numerical survey was not made for the year 1958-1959.

Foreign Medical School Graduates

During the academic year 1958-1959, 194 noncitizen residents were assigned to VA programs for limited periods of service averaging slightly less than five months. Of these, 171 served on a "without compensation" basis by assignment from university hospitals. Twenty-three were employed under contract privileges which are currently extended to noncitizens who are graduates of approved Canadian or American medical schools.

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A HISTORICAL NOTE ON THE ANNUAL REPORTS ON MEDICAL EDUCATION

WHEN the Council on Medical Education and Hospitals was formed in 1904 as a standing committee of the American Medical Association, one of the three general responsibilities it was charged to assume was "To make an annual report to the House of Delegates on the existing conditions of medical education in the United States." The report of the Council which appears in this issue of THE JOURNAL is in response to this early charge. However, the current report is the 59th of the series which obviously had its beginning prior to the formation of the Council.

The first Educational Number of THE JOURNAL appeared in 1901. Whether this was due to the interests and efforts of the Committee on Education which preceded the Council or was an independent venture of the editorial staff is not now clear. The initial report contained descriptive paragraphs which summarized the information found in the catalogs of 158 medical schools and presented statistical data in two tables. One was entitled "Medical Colleges of the United States," which portrayed for each school such matters as the numbers of students registered, the number of graduates and teachers, and the physician population ratio in the states concerned. The second table gave the geographical source of students enrolled.

Fourteen pages of the issue were devoted to a discussion of matters related to medical education. These matters were considered under such titles as: "University Work in Medicine," "Research Work for Undergraduates in Medical Schools," "Independence of Study and Thought in Medical Education," "The Elective System in the Medical School," "Value of the Fundamental Branches," "Changes in our Medical Schools Necessary to Meet Modern Conditions," and "The Medical College Association and Their Influence on Higher Standards of Medical Education."

The reader of the 59th Annual Report and other recent writings on medical education perhaps will share Whitman's thought quoted from his "Passage to India"—

> The past! the infinite greatness of the past!
> For what is the present after all, but a growth
> out of the past?

AN OPEN-ENDED MEDICAL EDUCATION

Many physicians are familiar with experiments in medical education which are designed, in part at least, to break the barrier that has traditionally existed between colleges and schools of medicine. The Hopkins experiment which went into effect this fall is but one example of several that either are planned or have been implemented. These programs allow selected students at the end of the second or third college year to begin medical school studies while at the same time continuing liberal arts college courses. Such experiments are being watched with interest, for they embrace the advantages not only of relating the medical school faculty and students more closely to the parent university but also of shortening by one year the formal educational span in medicine.

This effort to present medical study as a continuum of liberal arts study rather than to view each as separate segments, and on occasion as necessary hurdles, appears to be a principle that may be more widely applicable. Traditionally, education in medicine has been viewed as a series of distinct steps, i. e., college premedical study, medical school, internship, and residency training. Whether or not it will be possible to merge a part of college and medical school studies is dependent on the attitudes and actions not only of medicine but also of higher education in general. Medicine can, largely within itself, work toward a blending of all formal medical education.

There is a real unifying thread that binds together the segments of medical education beginning with the clinical clerkship in the third medical school year and running through the internship and residency programs. Throughout these various steps, there are the common and continuing objectives of providing students the opportunity to acquire clinical knowledge, skills, aptitudes, experience, wisdom, and judgment. The significant difference between the clerk, intern, and resident is largely one in degree of knowledge, skill, experience, and judgment which is reflected in the amount of responsibility delegated to the clerk, intern, or resident for patient care.

Viewed from this perspective, it is logical that the total clinical educational program should be constantly in mind as any of the stages within it are designed. Under these circumstances, each step can be planned to place particular emphasis where it should most logically rest. The clerkship could be fully developed to provide the student with a depth of knowledge of how clinical problems are rationally approached and resolved in the various clinical disciplines. The student could also acquire a beginning understanding of the particular diagnostic and therapeutic competences, techniques, and tools peculiar to major clinical disciplines. The depth of knowledge accompanied by only beginning responsibility for patient care at the student clerkship level would be replaced in the succeeding levels of internship and residency by greater breadth of knowledge and experience and greater patient responsibility.

By opening the early years of medical school study to allow for concomitant learning of college and medical disciplines, it is hoped that the two may better augment one another. It seems reasonable to expect that by opening the later years of medical school so that they may influence and be influenced more easily by the succeeding years of internship and residency, similar benefits may be obtained.

AMERICA'S RESPONSIBILITY TO THE FOREIGN MEDICAL GRADUATE

The recent Second World Conference on Medical Education, held under the auspices of the World Medical Association in Chicago, August 30-September 4, 1959, afforded the opportunity for discussion with leading medical educators from many nations. That the medical profession throughout the world looks toward the United States for leadership and assistance has been an important factor in bringing so many graduates from foreign medical schools to the United States for graduate medical education and training experiences during recent years.

Although some of the graduates of foreign medical schools have enjoyed excellent opportunities during their graduate medical education assignments in the United States, disappointment has been expressed by many others. There appear to be three general reasons why many foreign graduates have found their experiences disappointing, and even frustrating.

Many a foreign medical graduate has come to the United States to serve an internship in which he expected to obtain further education, but found that his real assignment was for basic service. Many a foreign medical graduate has found that whatever educational aspect was included in his program was a veneer so thin as to be almost nonexistent. The interest and concern of the hospital administration and of the professional staff in the service functions of the intern in such instances, and their feigned or almost complete absence of sincere interest or recognition of their responsibility to the foreign graduate, has been a genuine disappointment for many a young physician. Although this situation has been improving in recent years with the appointment of directors of medical education in many hospitals which are not integrated with teaching institutions, there is still much to be desired, in general. A hospital staff or administration that appoints foreign medical graduates should accept and be prepared to meet, because of the varied educational backgrounds and partial language barriers, an educational challenge even more demanding than that presented by graduates of our own schools.

The Educational Council for Foreign Medical Graduates now makes it possible to screen such persons prior to their house staff appointments. It will evaluate their medical credentials and test their knowledge of medicine and their command of English. Certification by the Educational Council for Foreign Medical Graduates will indicate that, on the basis of this screening, the individual possesses the background knowledge considered essential for appointment as an intern in a hospital approved for such graduate medical education. Thus the hospital administration and its professional staff now have a mechanism that should eliminate some of the inadequately prepared foreign graduates who have been accepted in the past and who, in some instances, were unable to benefit from their opportunities. However, with this mechanism the hospital administrators, boards of trustees, and professional staffs should recognize their responsibility and challenge to offer the foreign graduate whom they accept an educational experience worthy of American medicine and one that will serve him well when he returns to his own country.

A second cause for disappointment was expressed on the part of some who had received resident or fellowship appointments in some of the well-known teaching centers. Although some had enjoyed thoroughly excellent experiences, others had found that they were just part of a crowd. This latter group found that they were always on the periphery, looking on but never really participating. Participation in such instances seemed to be centered around the few favored persons who were destined to climb the pyramid to its apex. Highly competent foreign graduates have found this a disillusioning experience. Many of the graduates of our own schools have had similar experiences, so that this type of disappointment has, by no means, been restricted to foreign graduates. On the other hand, if our institutions and our educators in graduate medicine are to accept foreign physicians for such advanced education and training, it would appear that they have an obligation and challenge to afford these physicians the kind of opportunity that is meaningful and not just a grandstand side-line view. This general problem suggests the need for review of the current top-heavy graduate education program in some of our institutions.

The remaining cause for disappointment has been expressed by the foreign physician who has taken his complete graduate medical education and training in one of our approved residency programs and then found, in some instances, he was ineligible to be certified by the American specialty board concerned. A number of specialty boards currently admit properly qualified foreign medical graduates to their examinations with subsequent certification. However, well over half of the specialty boards have as eligibility requirements that the candidate should be a graduate of a medical school approved by the Council on Medical Education and Hospitals of the American Medical Association or that he should be a citizen of the United States. While this is sound policy for American citizens, it can almost nullify the possibility of certification of the foreign medical graduate. Such eligibility requirements have, therefore, made it impossible for some highly trained and otherwise completely qualified persons to obtain evidence, through American specialty board certification, of graduate educational experiences in the United States.

In times like these, when international understanding and cooperation are of paramount importance, it would appear highly desirable that restrictions of this type be given careful reconsideration. After all, the true function of a certifying agency, whether it be an American specialty board in the field of medicine or in some other area, should be the evaluation of the individual for competence in the field concerned and not concern with all of the details as to just how this competence has been developed. It is recognized that this latter contention may meet with difference of opinion, but from the objective point of view it would appear that some of the specialty boards are currently far too deeply involved in the details of the graduate educational experience and not sufficiently concerned with the total qualifications of the individual physician.

Has the time not arrived when all of the American specialty boards can, through the Advisory Board for Medical Specialties, reach a common agreement in regard to basic eligibility of the fully qualified foreign physician who has completed his specialty preparation in the United States? Such an agreement would remove one of the current barriers to international cooperation in the field of graduate medical education. It would make it possible for the well-qualified foreign physician to return to his homeland with the evidence he needs and should be privileged to enjoy. After all, a specialty certificate is not a license to practice but, rather, evidence of proficiency in a given field. This is an immediate challenge and sincere effort should be made to meet it.

THE BALANCE BETWEEN RESEARCH AND TEACHING IN MEDICAL SCHOOLS

All institutions of higher learning have in common the obligation to transmit and advance knowledge. The acceptance of dual responsibility of teaching and research in medical schools has posed in itself no serious problem, but the relationship between the two functions is not always as secure and comfortable as it should be. This has been particularly true in recent years, during which the ready availability of research funds has fostered great interest and growth in research activity.

Discussions about what constitutes a proper balance between these functions sometimes appears to indicate a belief that at worst research and teaching are antagonistic or at best that they are unhappy bedfellows. When these apparent beliefs are explored almost invariably they are denied, but still the controversy continues.

The attributes of critical intelligence, imaginative curiosity, controlled compassion, and a persistent will to find solutions to problems are equally basic and valuable to good students, teachers, investigators, and practitioners. The more of these separate identities that are merged into one individual the better will he perform his chosen task. Under these circumstances it would seem most natural that research and teaching should complement and strengthen one another.

In visiting many medical schools, one is impressed that this expected situation does not inevitably prevail. Initially it is not difficult to become convinced that the complementary relationship tends to suffer as the research effort of the school acquires bigness. Further experience makes it evident that the major factor is not the amount of research, the size of the grants or their sources, nor the number of investigators involved but rather the attitudes and interests of the faculty members responsible for the research which determine whether it shall complement and strengthen or dilute and weaken the teaching program.

As has been stated elsewhere research is one component of good teaching balance. Selection of faculty members capable of and dedicated to the two medical school obligations of teaching and research can assure that a favorable balance will be achieved.

MEDICINE'S GROWING DEPENDENCE ON ALLIED SCIENTISTS

The important role of the Ph.D. scientist as teacher and investigator in the basic medical sciences has long been recognized. Data presented by the Council on Medical Education and Hospitals in its current report indicate that almost 70% of full-time faculty members in the five major basic sciences do not hold the M.D. This represents a considerable decrease in the number of physician teachers in departments of anatomy, biochemistry, microbiology, pharmacology, and physiology since a similar analysis by Hinsey in 1950.[1] The greatest concentration of physician teachers in these subjects is in the most senior academic ranks so that the trend already clearly evident can be expected to continue.

The diminishing role of the physician in the basic science departments would be of serious consequence if it indicated that today's students have lost the opportunity to relate these disciplines to current clinical problems. There are three safeguards against this consequence: (1) the free interchange and easy communication that generally exist between basic science and clinical faculty; (2) the perceptiveness of students within whose minds the correlation of basic and clinical phenomena ultimately must take place; and (3) the increasing segment of career clinical teachers who have a sound background in one or more of the basic medical sciences as a necessary qualification for their own teaching and research.

Of even greater moment than the clinical orientation of these disciplines is that fundamental principles of the disciplines themselves, whether or not of current clinical significance, become a part of the student's knowledge. The important principles rather than facts of present clinical applications will provide the basis for understanding of future developments.

The impressive pace of medical advance gives ample proof that medicine's dependence on Ph.D. colleagues is well placed. The future will see an increase in the inherent interdependence of medicine and related sciences. The challenges posed will be met best as the relationships among all concerned continue to grow in mutual understanding and respect. The future will hold opportunities for increasing interdependence between medicine and related sciences and the rewards will be greatest as the relationships continue to grow in mutual understanding and respect.

MEDICOLEGAL INVESTIGATIONS

In The Journal September 1, 1956, page 40, under the heading Medical Examiner Versus Coroner System, a report was made of the then current legislative attempts to establish state medical examiner systems or to improve existing coroner systems. In 1954 the National Conference of Commissioners on Uniform State Laws approved a "Model Post-Mortem Examinations Act," which was the collaborative effort of the American Medical Association, the American Bar Association, the American Academy of Forensic Sciences, the American Judicature Society, the National Municipal League, and the National Civil Service League. At the time of the last report, the model law, or provisions similar to it, had been adopted in Massachusetts, Maryland, Virginia, Arkansas, Rhode Island, North Carolina, Georgia, Vermont, Louisiana, and parts of other states.

Since 1956 there has been considerable legislative activity but there have been relatively few enactments. Proposals patterned after the "model act" were introduced in many states but enacted in only one, Oregon, in 1959. According to a recent release of the National Municipal League relating to 1959 legislation in this field, the Oregon law creates a chief medical examiner in the state board of health and makes existing county or district health officers medical examiners. In other states: Iowa abolished the office of county coroner; Illinois created a centrally controlled autopsy service; Indiana created a Commission on Forensic Sciences; and North Carolina established a state toxicological laboratory. Qualified medical examiners have replaced elective coroners in parts of Florida, Michigan, New York, North Dakota, Pennsylvania, and Texas.

Many of the proposals that have been considered by the legislatures have been introduced and supported by local physicians and state medical society legislative committees. They are to be congratulated for giving their time in the interests of improving the quality of medicolegal investigations. It is to be hoped that the National Municipal League will continue its excellent work of acquainting legislators with the provision of, and need for, a model postmortem examinations act.

CHANGE OF ADDRESS

If you change your address please notify The Journal at least six weeks before the change is made. Include the address label clipped from your latest copy of The Journal, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

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MEDICAL NEWS

CALIFORNIA

Veterans Honor Dr. Geiger.—The National Commander of the Regular Veterans Association bestowed on Dr. Jacob C. Geiger, San Francisco, the Distinguished and Meritorious Service Ribbon and Gold Star in San Francisco, Oct. 28. The citation reads as follows: "For Valuable Medical and Public Health assistance rendered specifically to Veterans, over the many years; for services to this and other countries of the world and for being an outstanding citizen and public official."

DISTRICT OF COLUMBIA

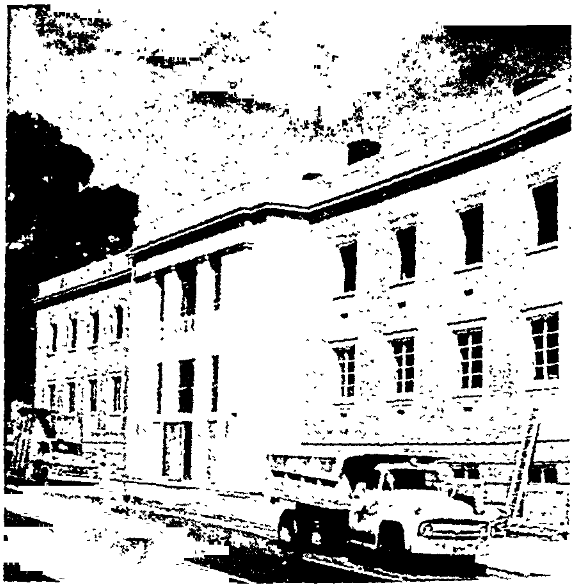
Annual Scientific Assembly.—The Medical Society of the District of Columbia will hold its 28th annual scientific assembly Nov. 23-25 at the Statler-Hilton Hotel, Washington, under the presidency of Dr. W. Leroy Dunn, who will open the meeting. The program is arranged as a schedule of 19 panel discussions. A clinicopathological conference the afternoon of Nov. 25 will be moderated by Dr. Louis B. Thomas, Seattle, head, surgical pathology and postmortem service, National Cancer Institute. A film-reading session is planned for the afternoon of Nov. 24, moderated by Dr. Fred O. Coe, chief of staff, Doctors Hospital, Washington. There is no registration fee. A society luncheon is planned for Nov. 23. Scientific and technical exhibits and motion pictures are planned.

INDIANA

State Medical Election.—Officers of the Indiana State Medical Association for 1959-1960 elected at 110th annual convention are: president-elect, Dr. Guy A. Owsley, Hartford City; treasurer, Dr. Okla W. Sicks, Indianapolis; assistant treasurer, Dr. Harry Pandolfo, Indianapolis. Delegates to the American Medical Association for a term ending Dec. 31, 1961, are Dr. Gordon B. Wilder, Anderson, and Dr. Wendell C. Stover, Boonville. Dr. Earl W. Mericle, Indianapolis, elected president-elect in October, 1958, was installed as president for 1959-1960.

MARYLAND

Dr. Heller Receives Cytology Award.—The Wien Award for 1958 was presented to Dr. John R. Heller, Bethesda, at a citation dinner Nov. 7. Each year, the Wien Award is presented to the scientist whose work or projects represent "outstanding research in cancer cytology." Initiated in 1953 by Leonard A. Wien, past-president of the Cancer Institute at Miami, the award consists of $1,000 and a bronze plaque. The first Wien Award was conferred on Dr. George N. Papanicolaou, New York City. Dr. Heller is director of the National Cancer Institute of the U. S. Public Health Service and earlier this year was appointed head of the cancer control section of the International Union Against Cancer.



Health Sciences Library on Baltimore Campus of the University of Maryland nears completion.

Library of Health Sciences.—Construction of the new Health Sciences Library on the Baltimore campus of the University of Maryland is nearing completion. The library, which will be ready for occupancy early in 1960, will serve the schools of dentistry, medicine, nursing, and pharmacy as well as University Hospital. The new million-dollar library consists of three stories and a basement. It will have space for 200,000 volumes, a study seating capacity for 400, and an auditorium that will seat 400. There will be individual study carrels, group study rooms, and faculty studies, in addition to the larger reading rooms. Historical collections of the four schools will be placed in a special room, arranged to show the development of each field separately.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

MASSACHUSETTS

Dr. Thorn Honored.—Dr. George W. Thorn, Boston, was the recipient of the 1959 Honor Award given by the American Medical Writers' Association. Dr. Thorn is professor of clinical medicine at Harvard University School of Medicine. The Honor Award is given from time to time to nonmembers of the association "who have made distinguished contributions in writing, editing, publishing, or other means of communication in medicine or allied sciences."

Personal.—Dr. Grete L. Bibring, associate clinical professor in psychiatry, Harvard Medical School, Boston, was elected vice-president of the International Psycho-analytic Association. Dr. Bibring is past-president of the Boston Psychoanalytic Society and Institute.——Dr. Charles C. Lund was appointed acting head of the Fifth Surgical Service and the Sears Surgical Laboratory at the Boston City Hospital. Dr. Lund, clinical professor of surgery in Harvard Medical School, was simultaneously appointed as acting head of the Harvard department of surgery at the Boston City Hospital.

Project to Train Psychiatric Aides.—A two-year project to train psychiatric aides at the Boston State Hospital in cooperation with the University's School of Medicine will be under the supervision of Dr. Walter E. Barton, Boston, associate professor of psychiatry at Boston University's School of Medicine and superintendent of Boston State Hospital. The project is supported by a $54,717 grant from the U. S. Department of Health, Education and Welfare, National Institute of Mental Health. Dr. Rufus M. Vaughn, of Amhurst, research assistant in psychiatry at the University of Massachusetts, is director of the project. A model ward of "chronically ill" mental patients will be set up with a team of specialists who will demonstrate to attendants how to develop interpersonal relationships and stimulate ward group activity. The aim of the program is "to shift the attitude and emphasis away from 'custodial care' toward the idea of a true 'therapeutic community.'"

MINNESOTA

Foreign Lecturer.—Dr. G. L. Montgomery, professor of pathology in the University of Edinburgh, Scotland, gave a lecture, "Chronic Thyroiditis," at the Mayo Clinic, Rochester, Oct. 9.

Institute to Study Water Resources.—An institute for the scientific study of the state's water resources including Lake Superior is being established at the University of Minnesota as a result of a Louis and Maud Hill Foundation grant of $207,721. The grant, accepted by the university board of regents on May 8, is for a period of five years. The limnological institute is an outgrowth of scientific studies made on Lake Superior and its tributaries by personnel in the University of Minnesota's School of Public Health under contract with the Minnesota Department of Health. The studies were financed by the Minnesota Water Pollution Control Commission. These studies of Lake Superior and its tributaries began in 1956 "to gain a better understanding of the full potential of Lake Superior from the standpoint of waste disposal, water supply, transportation, commercial fishing, tourist attractions, and other factors of economic importance to the state." Over-all project administration has been under the direction of Prof. Herbert M. Bosch, Minneapolis, with Prof. Theodore A. Olson, Minneapolis, in charge of technical work.

NEW YORK

Glaucoma Clinic in Schenectady.—The opening of a glaucoma detection clinic at St. Clare's Hospital, Schenectady, was held recently. The organization of the clinic was conducted by Dr. Peter Sykowski, chie[illegible] department, and will be under his [illegible] has been set up for families who can not afford a family eye physician. Patients will only be received by appointment which will be made through the social service director of the hospital.

New York City

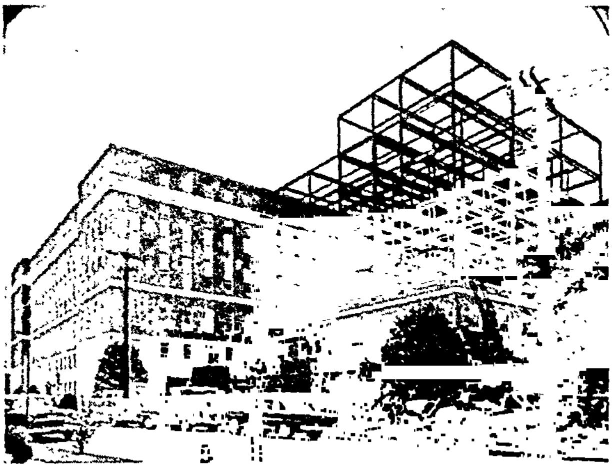
Fraternity Lecture.—Omicron Chapter of Phi Delta Epsilon Fraternity announced that Dr. Ralph A. Reis, Chicago, will give the Aaron Brown Memorial Lecture at New York Medical College, in the school auditorium, Tuesday, Nov. 24, at 4:30 p.m. His topic will be "Diabetes in Pregnancy."

Awards for Papers in Gastroenterology.—The American College of Gastroenterology announced the 1959 Ames Awards for "the best papers published during the past year" in its official publication, *The American Journal of Gastroenterology*. First prize went to Dr. Edward J. Nightingale for his paper, "Gastroenterological Aspects of Periarteritis Nodosa." The second prize was awarded to Drs. Abraham J. Brenner, Adolph Kornstein, Martin Bandler, and Milton J. Matzner, of Brooklyn, for their paper, "Present Status of Gastric Cytology." The third prize was given to Dr. Burrill B. Crohn for "Regional Ileitis, Ileojejunitis, Combined Ileocolitis."

Directory of Health Services.—"How to Secure Help for Those Who Need It," a free 32-page directory to information services in the welfare and health field in New York City, has been published by the Community Council of Greater New York. The booklet is designed to help people find the proper agency for their problem. It lists information services on every welfare and health topic including adoption, alcoholism, the blind, camps, child guidance, convalescent care, drug addiction, employment, and vocational counselling, public assistance, housing, mental health, nursing homes, social security, rehabilitation, travelers, unmarried mothers, and veterans. Copies are available to individuals who send a stamped, self-addressed envelope with their request to the Information Bureau Community Council of Greater New York, 345 East 45th St., New York 17. The booklet will be distributed to all city policemen, physicians, taxi cab drivers, lawyers, librarians, personnel directors, and others "who come in daily contact with persons who may need help."

NORTH CAROLINA

Dedicate Medical School Addition.—In observance of the 20th anniversary of the founding of the Bowman Gray School of Medicine of Wake Forest College, Winston-Salem, the school's new 2-million-dollar addition was dedicated Oct. 23. Known as the James A. Gray Memorial Building, the five-story structure more than doubles space previously available to the school since its completion in 1941. The Gray Memorial Building honors the late brother of the man for whom the school is named. A former president and chairman of the board of directors of R. J. Reynolds Tobacco Co., James A. Gray was for many years a benefactor of the school endowing it with one million dollars. The opportunity to transform the two-year Wake Forest Medical School, founded in 1902, into a four-year school was afforded by a bequest from the late Bowman Gray, at his death chairman of the board of directors of R. J. Reynolds Tobacco Co. Dr. C. C. Carpenter, who in 1935 became dean of the two-year Wake Forest Medical School, has continued as dean of Bowman Gray. Judge Hubert E. Olive, of Shelby, president of the Wake Forest board of trustees, presided at the dedication. The entire James A. Gray Memorial Building was open to the public Oct. 22-23, and special exhibits and demonstrations of aids and techniques used in medical education were shown.



The new James A. Gray Memorial Building of Bowman Gray School of Medicine, Winston-Salem. In the foreground is the Research Center being constructed with funds derived from a campaign among the medical alumni.

TEXAS

Grant for Research in Genetics.—The University of Texas has received a grant of $1,482,480 for basic research in genetics and cell biology over a five-year period. The grant, from the National Institutes of Health, the Public Health Service research center of Bethesda, Md., will support research in the areas of population genetics; genetic effects of radiation and cosmic rays; chromosome studies of cancer and normal cell strains; cytogenetics; and the physiological and biochemical aspects of genetics. Principal investigators will be Wilson S. Stone, Ph.D., Austin, zoology department chairman; and Clarence P. Oliver, Ph.D., Austin; Robert P. Wagner, Ph.D., Austin; John J. Biesele, Ph.D., New York City; Marshall R. Wheeler, Ph.D., Austin; Burke H. Judd, Ph.D., Austin; and Hugh S. Forrest, Ph.D., Pasadena, Calif., of the university's genetics and cell biology group. The university was selected for the grant by the National Advisory Health Council.

WEST VIRGINIA

Unit for Cardiac Work Classification.—Mr. F. Ray Power, Charleston, state director of the division of vocational rehabilitation, announced that West Virginia's first cardiac work classification unit will begin operation at Institute during November. The facility is being sponsored in cooperation with the Kanawha Medical Society, the Kanawha Heart Association, and the West Virginia Heart Association. The unit is designed to assess the potentials of persons with definitely diagnosed cardiac conditions. It is for evaluation purposes only and will in no way serve as a diagnostic or treatment facility for persons with suspected heart conditions. Referrals will be through the Vocational Rehabilitation Division and private physicians throughout the state. Two Charleston physicians, Dr. William C. Stewart and Dr. William C. Revercomb, Jr., will serve on the staff's evaluation team, together with Miss Arla Tucker, a registered nurse technician. A vocational counselor and a social worker will be added as members of the staff.

GENERAL

Surgeons Meeting in Las Vegas.—The International College of Surgeons, United States Section will hold its second western surgical meeting in Los Vegas, Nev., at the Star Dust South Hotel, Nov. 22-24. A total of 15 papers is scheduled on the program. A luncheon panel, "Intestinal Surgery," is planned for noon, Nov. 23, and a general luncheon panel will be held Nov. 24. Exhibits and motion pictures are planned. On the evening of Nov. 23 a banquet will be held. Registration fee is $25. A ladies' program is arranged. For information write Dr. Frederick M. Turnbull Jr., 1930 Wilshire Blvd., Los Angeles 57, Secretary.

Medical Conference in Nassau.—The eighth Bahamas Medical Conference will be held Nov. 27-Dec. 17 in Nassau, Bahamas, with headquarters at the British Colonial Hotel. The program includes over 20 speakers and more than 45 papers. Dr. P. David Wheatley, vice-president, section of general practice, Royal Society of Medicine, London, England, will present "The English National Health Scheme" the morning of Nov. 29. Mr. Marlin E. Lerch, eastern director of public relations, Household Finance Corporation, Philadelphia, will present "The Littlest Giant—Your Patient; His Financial Needs Can be Solved" Dec. 6. The ninth Bahamas Medical Conference will be held April 1-14, 1960. For information, write Mr. Irvin M. Wechsler, General Manager, Bahamas Conferences, P. O. Box 1454, Nassau, Bahamas.

Hematology Meeting in St. Louis.—The second annual meeting of the American Society of Hematology will be held Nov. 22-24 in St. Louis. Papers on antibody synthesis will be presented the morning of Nov. 23 with the following titles and participants:

The Acquisition of Immunologic Specificity, Fred Karush, Ph.D., Philadelphia.
"Selection" versus "Instruction" in the Synthesis of Antibodies, Dr. David W. Talmage, Denver.
Antibody Production by Single Cells, Edwin S. Lennox, Ph.D., Ann Arbor, Mich.
Studies on Antibody Synthesis, Dr. Albert H. Coons, Boston.
Immune Tolerance and Autoimmune Disease, Rupert E. Billingham, Ph.D., Philadelphia.

Other major program subjects include, viral etiology, chemical and hormonal factors, and genetics. On Nov. 24 general papers will be presented from the membership at large. For information, write Dr. John W. Rebuck Henry Ford Hospital, Detroit, Secretary.

Dr. Flexner Dies.—The founder and first director of the Institute for Advanced Study at Princeton, N. J., Dr. Abraham Flexner, died Sept. 21 at age 92. Born Nov. 13, 1866, in Louisville, Ky., Dr. Flexner was appointed by Mr. Henry S. Pritchett, head of the Carnegie Foundation for the Advancement of Teaching, to direct an investigation of medical schools that led to the Flexner Report, "Medical Education in the United States and Canada," in 1910. Dr. Flexner visited 155 medical colleges in the United States and Canada. From 1913 to 1929 he served on the staff of the General Education Board and used the office to enlist the elder John D. Rockefeller, its benefactor, in his efforts to revamp medical education. In 1930 Dr. Flexner came out of his first retirement to organize the Institute of Advanced Study. He was awarded the degree of M.D., honoris causa, from the University of Berlin and the University of Brussels.

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, it territories and possessions in the weeks ended as indicated:

Area	Oct. 17, 1959		Oct. 18 1958
	Paralytic Type	Total Cases	Total
New England States			
Maine	7	7	..
New Hampshire	..	..	..
Vermont	3	3	..
Massachusetts	5	6	..
Rhode Island	..	..	..
Connecticut	2	2	2
Middle Atlantic States			
New York	20	35	15
New Jersey	7	7	9
Pennsylvania	10	10	4
East North Central States			
Ohio	1	6	36
Indiana	3	5	6
Illinois	7	11	9
Michigan	6	20	66
Wisconsin	..	3	3
West North Central States			
Minnesota	11	14	3
Iowa	3	6	..
Missouri	9	18	6
North Dakota	..	1	1
South Dakota	..	..	..
Nebraska	1	2	2
Kansas	2	2	3
South Atlantic States			
Delaware	..	1	3
Maryland	7	7	3
District of Columbia	..	..	..
Virginia	13	13	10
West Virginia	7	7	10
North Carolina	15	15	3
South Carolina	1	3	1
Georgia	2	2	..
Florida	1	1	9
East South Central States			
Kentucky	2	2	2
Tennessee	11	13	8
Alabama	5	5	2
Mississippi	5	5	11
West South Central States			
Arkansas	5	7	1
Louisiana	..	..	4
Oklahoma	2	4	2
Texas	8	10	19
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	2	2	..
New Mexico	..	..	2
Arizona	..	..	..
Utah	..	..	1
Nevada	..	..	..
Pacific States			
Washington	17	17	5
Oregon	8	10	1
California	17	18	23
Alaska	..	..	..
Hawaii	..	..	2
Territories and Possessions			
Puerto Rico	..	..	1
Total	225	300	288

Program for Research in Sex.—The Division of Medical Sciences of the National Academy of Sciences–National Research Council is accepting applications for grants-in-aid on research for consideration by the Committee for Research Problems of Sex. The funds for support of this program are provided by the Rockefeller Foundation and the Ford Foundation. The committee is concerned primarily with encouraging research on the mechanisms underlying sexual behavior, with special emphasis on the higher mammal and man. Proposals involving endocrinological, neurological, psychological, anthropological, phylogenic, and genetic studies are invited. Requests that deal with the physiology of reproduction or with related biological and biochemic fields should be addressed to the committee "only if they give promise of shedding light upon behavioral mechanisms." Inquiries should be addressed to Room 411, Division of Medical Sciences, National Academy of Sciences–National Research Council, 2101 Constitution Ave., N. W., Washington 25, D. C. Completed applications for 1960-1961 should be postmarked on or before Jan. 15, 1960.

Commission of Neurochemistry.—The Commission of Neurochemistry of the World Federation of Neurology met for the first time at the Institut Bunge in Antwerp, Belgium, Sept. 29-30. Dr. Ludo van Bogaert, Antwerp, president of the federation, and Dr. Charles M. Poser, Kansas City, Kan., medical executive officer, assisted at the meeting. The commission discussed the participation of neurochemists in the different international congresses. A permanent secretariat is to be established at the Institut Bunge, in Antwerp. Dr. A. Lowenthal, Antwerp, was named secretary. Plans were laid for holding a "Symposium on Neurochemistry" in Rome during the Congress on Neurology of 1961. The major topics to be covered are (1) lipids, lipoproteins and their metabolism; and (2) disorders of myelin (not including disseminated sclerosis). The commission plans to establish a registry of neurological material available for neurochemical investigation. Requests and inquiries should be addressed to the secretary of the commission.

Fellowships for Research.—The National Science Foundation announced the award of 35 fellowships for advanced study and research in the sciences in the foundation's Postdoctoral Fellowship Program. All awards were approved by the National Science Board upon the recommendation of Alan T. Waterman, Ph.D., Washington, D. C., director of the foundation. Fellows were selected "on the basis of ability as evidenced by letters of recommendation, academic records, and other evidence of scientific attainment." Final selection of fellows was made by the National Science Foundation. The postdoctoral fellows received an annual stipend of $4,500, an allowance for dependents, and a limited allowance to aid in defraying the cost of travel to the affiliated institution. These awards will enable the recipients to study or carry on their research at 18 institutions in the United States and in 17 foreign institutions. The National Science Foundation is accepting applications for awards to be made in March, 1960, in its graduate and postdoctoral fellowship programs. For information, write the National Science Foundation, 1951 Constitution Ave., N. W., Washington 25, D. C.

Society News.—At its 13th general assembly the **World Medical Association** elected the following officers: president, 1959-1960, Dr. Renaud Lemieux, Canada; president-elect, 1959-1960, Dr. Paul Eckel, Germany; members of council, 1959-1962, Dr. Romeo Y. Atienza, Philippines; Dr. Gunnar Gunderson, La Crosse, Wis.; Dr. A. P. Mittra, India; and Dr. M. Poumailloux, France.——The **American Academy of Physical Medicine and Rehabilitation** elected the following officers for 1959-1960: president, Dr. Clarence W. Dail, Los Angeles; president-elect, Dr. Ray G. Piaskoski, Milwaukee; vice-president, Dr. Robert W. Boyle, Milwaukee; secretary, Dr. Harriet E. Gillette, Gainesville, Fla.; treasurer, Dr. James W. Rae Jr., Ann Arbor, Mich.; and executive secretary, Mrs. Dorothea C. Augustin, Chicago.——Dr. Harold G. Reineke, Cincinnati, was named president-elect of **American Roentgen Ray Society**, succeeding Dr. Edward B. D. Neuhauser, Boston, who became society president. Dr. Reineke assumes the presidency in 1960. Other officers elected include Dr. C. Allen Good, Rochester, Minn., secretary, and Dr. Robert K. Arbuckle, Oakland, Calif., treasurer. Dr. John F. Holt, Ann Arbor, Mich., was elected chairman of the executive council. The society's 1960 meeting will be held Oct. 4-7 in Atlantic City at the Ambassador Hotel.

CANADA

Physicians Meet in Winnipeg.—The American College of Physicians will hold a Prairie Regional Meeting for Manitoba, Saskatchewan, and Alberta at the Auditorium of the Faculty of Medicine, University of Manitoba, and Fort Garry Hotel, Winnipeg, No. 20-21. Dr. Percy H. Sprague, governor of the college for Alberta, will open the program with an address. The following papers include invited participants:

Pulmonary Hypertension, Dr. Richard E. Rossall, Edmonton.
Hypertension in the Male, Dr. Ashley E. Thomson, Winnipeg.
Thyroid Disease, Dr. John P. Gemmell, Winnipeg.
Use of Fluorescent Antibody Technique in the Diagnosis of Systemic Lupus, Dr. Charles Baugh, Saskatoon.
Macroglobulinaemia—Its Clinical Implications, Drs. David E. Rodger and S. R. Meighen, Regina.
Recognition and Diagnosis of Metabolic Bone Disease, Dr. George Jaworski, Saskatoon.
Diabetes and Pregnancy, Dr. Morris Bertrand, Edmonton.
Assessment of Mitral Regurgitation, Dr. Charles P. Newcombe, Rochester.

Dr. Irving S. Wright, New York City, will be the speaker at the evening dinner, presenting "The Role of the American College in Internal Medicine." For information, write Dr. John F. S. Hughes, 326 Medical Arts Building, Winnipeg, Manitoba, Canada.

CORRECTIONS

Hypertension, Pregnancy, and Pheochromocytoma. –In the Sept. 12 issue on page 151, the clause beginning on line 13 under Report of Cases should have read "labor was induced with intravenously given oxytocin (Pitocin)."

Newer Concepts of Jaundice.–In the Oct. 24 issue, in the editorial on page 1110, right-hand column, the sentence beginning on line 11 should have read "Dutton and Storey[3] demonstrated that the synthesis of uronides in the liver is dependent on the presence of two factors, a heat-stable coenzyme and a heat-labile enzyme." Line 25 should have read "and amines. Included are drugs, e. g., salicylates." In the last paragraph the word "unronide" should have read "uronide."

EXAMINATIONS AND LICENSURE

EDUCATIONAL COUNCIL FOR FOREIGN MEDICAL GRADUATES, INC.

Educational Council for Foreign Medical Graduates: Stations around the world. March 16, 1960 and Sept. 21, 1960. Exec. Director, Dr. Dean F. Smiley, 1710 Orrington Ave., Evanston, Ill.

NATIONAL BOARD OF MEDICAL EXAMINERS

National Board of Medical Examiners: Part I, Various Cities, June 21-22 and Sept. 7-8. Part II, Various Cities, April 19-20. Applications must be received at least six weeks before the date of the examination. Exec. Sec., Dr. John P. Hubbard, 133 South 36th St., Philadelphia.

BOARDS OF MEDICAL EXAMINERS

Alabama: *Examination*. Montgomery, June 21-23, 1960. Sec., Dr. D. G. Gill, State Office Bldg., Montgomery.

Alaska:* On application in Anchorage or Fairbanks. Sec., Dr. W. M. Whitehead, 172 South Franklin St., Juneau.

California: *Oral*. San Francisco, November 14. *Oral and Clinical*. San Francisco, Nov. 15. Sec., Dr. Lous E. Jones, Room 536, 1020 N Street, Sacramento.

Colorado:* *Examination*. Denver, Dec. 8-9. *Reciprocity*. Denver, Oct. 14. Exec. Sec., Miss Mary M. McConnell, 715 Republic Bldg., 1612 Tremont Place, Denver 2.

Delaware: *Examination*. Dover, Jan. 12-14. *Endorsement*. Dover, Jan. 21. Sec., Dr. Joseph S. McDaniel, Professional Bldg., Dover.

District of Columbia:* *Examination*. Washington, Dec. 14-15. *Reciprocity*. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Florida:* *Examination*. Miami Beach, Nov. 22-24. Sec., Dr. Homer L. Pearson, 901 N.W. 17th St., Miami 36.

Guam: *Subject to Call*. Act. Sec., Dr. F. L. Conklin, Agana.

Hawaii: *Examination*. Honolulu, Jan. 11-12. Sec., Dr. I. L. Tilden, 1020 Kapiolani St., Honolulu.

Idaho: *Examination* and *Reciprocity*. Boise, Jan. 11, 12, 13. Exec. Sec., Mr. Armand L. Bird, 364 Sonna Bldg., Boise.

Indiana: *Examination*. Indianapolis, June 1960. *Reciprocity*. Indianapolis, fourth Wednesday of each month. Ex. Sec., Miss Ruth V. Kirk, 538 K. of P. Bldg., Indianapolis.

Kansas:* *Examination and Reciprocity*. Kansas City, Jan. 15-16. Sec., Dr. F. J. Nash, New Brotherhood Bldg., Kansas City.

Kentucky: *Examination*. Frankfort, Dec. 14-15. Asst. Sec., Mrs. Ray Wunderlich, 620 South Third St., Louisville 2.

Louisiana: *Examination and Reciprocity*. New Orleans, Dec. 3-5. Sec., Dr. Edwin H. Lawson, 930 Hibernia Bank Bldg., New Orleans 12.

Maryland: *Examination*. Baltimore, Dec. 8-11, Sec., Dr. Frank K. Morris, 1211 Cathedral St., Baltimore 1.

Massachusetts: *Examination*. Boston, Jan. 12-15. Sec., Dr. David W. Wallwork, Room 37, State House, Boston.

Minnesota:* *Examination*. Jackson, June 1960. *Reciprocity*. Jackson, Dec. 7, Sec., Dr. A. L. Gray, Old Capitol, Jackson.

Nebraska:* *Examination*. Omaha, June 13-15, 1960. Dir., Bureau of Examining Boards, Room 1009, State Capitol Bldg., Lincoln 9.

New Jersey: *Examination*. Jan. 19-22. *Reciprocity*. Monthly, Sec., Dr. Royal A. Schaaf, 28 West State St., Trenton.

New Mexico:* *Examination and Reciprocity*. Santa Fe, Nov. 16-17. Sec., Dr. C. Derbyshire, 227 East Palace Ave., Santa Fe.

New York: *Examination*. Albany, Buffalo, New York and Syracuse, Dec. 8-11. Sec., Dr. Stiles D. Ezell, 23 South Pearl St., Albany.

North Dakota: *Examination*. Grand Forks, Jan. 6-8. *Reciprocity*. Grand Forks, Jan. 9. Sec., Dr. C. J. Glaspel, Box 228, Grafton.

Ohio: *Examination*. Columbus, Dec. 15-17. *Endorsement*. Columbus, Oct. 5. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

Pennsylvania: *Examination*. Philadelphia, January. Sec., Mrs. Margaret G. Steiner, Box 911, Harrisburg.

South Carolina: *Examination and Endorsement*. Columbia, Dec. 8. Sec., Dr. H. E. Jervey, Jr., 1329 Blanding St., Columbia.

Texas:* *Examination*. Fort Worth, Dec. 3-5. Sec., Dr. M. H. Crabb, 1714 Medical Arts Bldg., Fort Worth 2.

Utah: *Examination*. Salt Lake City, July 6-8. *Reciprocity*. Salt Lake City, Nov. 17. Director, Mr. Frank E. Lees, 324 State Office Bldg., Salt Lake City 1.

Virginia: *Reciprocity*. Dec. 1, *Examinations* Dec. 2-4 inclusive, Richmond. Address: Board of Medical Examiners, 631 First St. S. W., Roanoke.

Washington:* *Examination*. Seattle, Jan. 11-13. Administrator, Professional Division, Capitol Bldg., Olympia.

West Virginia: *Examination*. Charleston, January. Sec., Dr. Newman H. Dyer, State Office Bldg., No. 3, Charleston 5.

Wisconsin:* *Examination*. Madison, Jan. 14-16. Sec., Dr. Thomas W. Tormey, Jr., 1140 State Office Building, 1 West Wilson St., Madison.

Wyoming: *Examination and Reciprocity*. Cheyenne, Feb. 1. Sec., Dr. James W. Sampson, State Office Bldg., Cheyenne.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Alaska: *Examination and Reciprocity*. Juneau, November. Sec., Dr. R. Harrison Leer, Alaska Office Bldg., Juneau.

District of Columbia: *Examination*. Washington, Nov. 23-24. Deputy Director, Mr. Paul Foley, 1740 Massachusetts Ave., Washington 6.

Rhode Island: *Examination*. Providence, Nov. 18. *Reciprocity*. Providence, Nov. 4. Administrator, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

South Dakota: *Examination*. Vermillion, Dec. 4-5. Dr. Gregg M. Evans, 310 East 15th St., Yankton.

Washington: *Examination*. Seattle, Jan. 6-7. Sec., Mr. Thomas A. Carter, Capitol Bldg., Olympia.

Wisconsin: *Examination*. Milwaukee, Dec. 5, Madison, Apr. 9, Sec., Mr. Wm. H. Barber, 621 Ranson St., Ripon.

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*Basic Science Certificate required.

DEATHS

Arnold, Elmer William Ⓜ Adrian, Minn.; University of Nebraska College of Medicine, Omaha, 1907; member of the American Academy of General Practice; veteran of World War I; formerly mayor of Bigelow; served as president of the school board, the Southwestern Minnesota Medical Society, and the Sioux Valley Medical Association; surgeon for the Northwestern Railroad; the Dr. Arnold Memorial Hospital was named in his honor; died Sept. 2, aged 77.

Bailey, Edward B. Ⓜ Wichita Falls, Texas; Baltimore Medical College, 1909; formerly practiced in Austin; died Aug. 22, aged 73.

Baird, Homer Dale Ⓜ Montreal, Wis.; University of Pennsylvania School of Medicine, Philadelphia, 1911; member of the Industrial Medical Association; for many years on the staff of the York (Pa.) Hospital; died in the Trinity Hospital, Ashland, Aug. 25, aged 69.

Beigler, Sydney Karl Ⓜ Detroit; University of Michigan Medical School, Ann Arbor, 1924; at one time taught at the University of Wisconsin Medical School in Madison; fellow of the American College of Surgeons; on the staffs of the Sinai and Harper hospitals; died Sept. 5, aged 60.

Benton, Charles Crisp Ⓜ Macon, Ga.; born in Monticello May 30, 1919; University of Georgia Medical Department, Augusta, 1944; specialist certified by the American Board of Anesthesiology; member of the American Society of Anesthesiologists, Inc.; interned at the Jefferson and Hillman Hospital in Birmingham, Ala.; served a residency at the Crawford W. Long Memorial Hospital in Atlanta, Ga., and the University Hospital in Augusta, Ga.; served as a lieutenant commander in the medical corps of the U. S. Naval Reserve; associated with the Macon, Parkview, Middle Georgia, and St. Luke hospitals; died Aug. 22, aged 40.

Bintakys, Fricas Martynas, Brooklyn; Vytauto Didziojo Universiteto Medicinos Fakulteto, Kaunas, Lithuania, 1941; interned at the Prospects Heights Hospital; died Sept. 3, aged 48.

Boggs, Nathan Ⓜ Goodwell, Okla.; Rush Medical College, Chicago, 1906; veteran of World War I; for many years practiced in Oklahoma City, where he served a term as trustee of the Oklahoma City University, and was on the staff of the Wesley Hospital; at one time on the faculty of the University Medical College in Kansas City, Mo.; from 1952 to 1957 on the medical staff of the Panhandle A. & M. College; died in the Guymon (Okla.) Municipal Hospital Aug. 31, aged 80.

Bowman, Douglas Clyde Ⓜ Naches, Wash.; Washington University School of Medicine, St. Louis, 1928; member of the American Academy of General Practice; died in the Yakima Valley Memorial Hospital Aug. 29, aged 58.

Brown, Clarence Morgan, Adairville, Ky.; University of Tennessee Medical Department, Nashville, Tenn., 1898; died in the Baptist Hospital, Nashville, Tenn., Aug. 15, aged 84.

Camp, Donald Evans, West Union, Iowa; State University of Iowa College of Medicine, Iowa City, 1924; veteran of World War II; died in Detroit Aug. 28, aged 62.

Camp, Harold Manlove Ⓜ Monmouth, Ill.; born in Brooklyn, Ill., July 24, 1885; Northwestern University Medical School, Chicago, 1909; councilor from 1922 to 1924 of the Fourth District of the Illinois State Medical Society of which he was secretary from 1924 to 1942, when he became secretary treasurer; from 1912 to 1924 secretary of the Warren County Medical Society; served as president of the National Conference on Medical Service, formerly the Northwest Regional Conference, of which he was secretary; served as vice-president of the Aero Medical Association; first medical examiner for the Civil Aeronautics Administration in Monmouth; in 1937 appointed a member of the committee to the then newly created advisory board of the Division for Handicapped Children, State Department of Public Welfare; formerly member of the House of Delegates of the American Medical Association; past-president of the Monmouth Medical Club; member of the World Medical Association; an honorary member of the Fifty Year Club of the Texas Medical Association; during World War II, served as state chairman for Procurement and Assignment Service for Physicians under the War Manpower Commission; on Sept. 24, 1959 the Warren County Medical Society and the Monmouth Medical Club honored him; the occasion marked his fifty years as a physician; in June 1958 Northwestern University honored him with a Merit Award; past-president of the Monmouth Rotary Club; on the staff of the Monmouth Hospital; in September 1959 honored by the Chicago, Burlington and Quincy Railroad for his many hundred miles of traveling, commuting between the offices of the Illinois State Medical So-

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Ⓜ Indicates Member of the American Medical Association.

ciety in Chicago and Monmouth; since 1941 editor of the *Illinois State Medical Journal*; died in St. Mary's Hospital, Galesburg, Oct. 17, aged 74.

Carroll, Harry Roland, Baltimore; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1917; veteran of World War I; formerly associated with the U. S. Public Health Service, serving for many years as director of the Custom House out-patient annex of the U. S. Public Health Service Hospital, where he died Sept. 7, aged 65.

Colwell, John Bruner Ⓜ Champaign, Ill.; Rush Medical College, Chicago, 1902; from 1904 to 1911 assistant warden at the Cook County Hospital in Chicago; served as attending physician on the staff of the Cunningham Children's Home in Urbana; on the staff of the Burnham City Hospital; died in the Carle Memorial Hospital in Urbana Sept. 17, aged 86.

Comfort, John Burke, Trenton, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1919; past-president of the Mercer County Medical Society; veteran of World War I; on the staff of St. Francis Hospital, where he died Aug. 27, aged 66.

Darling, Earl H., Milwaukee; Wisconsin College of Physicians and Surgeons, 1907; associated with St. Mary's and Columbia hospitals; died Aug. 25, aged 76.

Dillingham, Frank Stinson Ⓜ Los Angeles; University of Southern California College of Medicine, Los Angeles, 1900; specialist certified by the American Board of Urology; member of the American Urological Association and served as secretary of the Western Branch; for many years on the staff of the California Hospital; died in St. John's Hospital in Santa Monica Aug. 31, aged 80

Donnelly, James Herbert Ⓜ Buffalo, N. Y.; McGill University Faculty of Medicine, Montreal, Que., Canada, 1906; specialist certified by the American Board of Internal Medicine; member of the American College of Chest Physicians; fellow of the American College of Physicians and past president of the New York State Chapter; past-president of the Buffalo Academy of Medicine; member of the Catholic Physicians Guild; served on the faculty of the University of Buffalo School of Medicine; for many years director of tuberculosis for the city health department; examiner for the Selective Service during World War I; honorary consultant at the Edward J. Meyer Memorial Hospital and Sisters of Charity Hospital, where he died Aug. 31, aged 84.

Dunn, Burton Leonard, Babylon, N. Y.; Syracuse University College of Medicine, 1897; died in the Oneida City Hospital in Oneida Aug. 24, aged 88.

Dunscombe, William Colby Ⓜ Mayaguez, P. R.; American Medical Missionary College, Battle Creek, Mich., and Chicago, 1906; L.R.C.P. and L.R.C.S., of Edinburgh, and L.R.F.P.&S., of Glasgow, Scotland, 1912; for many years a medical missionary; served with the U. S. Public Health Service; at one time superintendent of the Wabash Valley Sanitarium in Lafayette, Ind.; died Aug. 24, aged 78.

Egenolf, George Franklin Ⓜ San Diego, Calif.; born in Orange, N. J., July 6, 1920; Stanford University School of Medicine, San Francisco, 1945; interned at the Naval Hospital in San Diego; served a residency in pathology at St. Vincent's Hospital in Los Angeles; served a residency in surgery and obstetrics and gynecology at the San Diego County General Hospital; veteran of World War II; specialist certified by the American Board of Obstetrics and Gynecology; associated with the Scripps Memorial Hospital in La Jolla and the Sharp Memorial Hospital and Mercy Hospital; died in La Paz, Baja California, Mexico, Aug. 21, aged 39.

Etheridge, Isaac Holder, Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1917; for many years county physician; trustee of Ardmore Children's Convalescent Hospital; associated with the Jesse Parker Williams Hospital and the Crawford W. Long Memorial Hospital, where he died Aug. 26, aged 71.

Evans, Alexander Leon, Brooklyn; Universität Bern Medizinische Fakultät, Switzerland, 1935; member of the American Academy of General Practice; veteran of World War II; served on the staffs of the Doctors Hospital in New York City, Coney Island, Madison Park, Kingshighway, and Brooklyn hospitals; died Sept. 10, aged 49.

Evans, Mary Louise, Doylestown, Pa.; Woman's Medical College of Pennsylvania, Philadelphia, 1906; died in New Britain June 15, aged 77.

Foster, Maude Elizabeth Ⓜ Atlanta, Ga.; Medical College of South Carolina, Charleston, 1922; died July 30, aged 75.

Fox, Carl Alexander Ⓜ Birmingham, Ala.; Medical Department of Tulane University of Louisiana, New Orleans, 1900; served on the staff of the Children's Hospital; died in Woodmere, N. Y., Aug. 20, aged 80.

Freeman, Robert Herman, Raleigh, N. C.; Jefferson Medical College of Philadelphia, 1908; died in the Rex Hospital Aug. 22, aged 74.

Frenkiel, Henry Ⓜ New York City; Uniwersytet Jozefa Pilsudskiégo, Warszawa, Poland, 1925; interned at the Fordham Hospital, where he served a residency; formerly a resident at the Roosevelt Hospital in New York City and the Kings County Hospital in Brooklyn; died June 14, aged 64.

Gibson, William John Ⓜ Hollywood, Fla.; University of Buffalo School of Medicine, 1917; for many years practiced in Rochester, N. Y.; veteran of World War I; died Sept. 6, aged 72.

Glassman, Joseph Ⓜ New York City; University and Bellevue Hospital Medical College, New York City, 1915; executive director and chief of internal medicine at Stuyvesant Polyclinic and consulting physician at the Italian Hospital; died Sept. 10, aged 76.

Goode, John William Ⓜ San Antonio, Texas; University of Texas School of Medicine, Galveston, 1912; fellow of the American College of Surgeons; past-president of the Bexar County Medical Society; associated with the Baptist Memorial Hospital and the Nix Memorial Hospital; died Aug. 30, aged 73.

Gutierrez, Juan Bautista, Brownsville, Texas; Universidad Nacional Facultad de Medicina, México, D. F., 1913; died in the Mercy Hospital June 15, aged 76.

Heilbrunn, Max Ⓜ Lockwood, Mo.; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1924; interned at the Menorah Hospital in Kansas City, Mo.; associated with the Lockwood Memorial Hospital, where he died Aug. 26, aged 62.

Herbst, Frank Ⓜ Kansas City, Mo.; Harvard Medical School, Boston, 1901; died July 26, aged 81.

Jackson, Henry Bruce, Newnan, Ga.; Hospital Medical College, Eclectic, Atlanta, 1909; died in the Newnan Hospital July 28, aged 73.

Jefferson, Charles William Ⓜ Louisville, Ky.; University of Louisville Medical Department, 1910; served in the medical corps of the American and British armies during World War I; member of the Southeastern Surgical Congress and the Industrial Medical Association; fellow of the International College of Surgeons; past-president of the staffs of the Jewish Hospital and St. Anthony Hospital, where he died Sept. 2, aged 70.

Johnson, Marvin Anthon Ⓜ Plainview, Neb.; University of Nebraska College of Medicine, Omaha, 1935; interned at the Douglas County Hospital in Omaha; member of the American Academy of General Practice; died in the Plainview General Hospital Aug. 19, aged 49.

Jones, Harold Walter Ⓜ Philadelphia; born in Newark, N. J., Feb. 1, 1891; Jefferson Medical College of Philadelphia, 1917; specialist certified by the American Board of Internal Medicine; professor of clinical medicine, emeritus, at his alma mater, where he was the first person to hold the Thomas Drake Martinez Cardeza Chair of clinical medicine and hematology established in 1941; member of the Association of American Physicians; fellow of the American College of Physicians; founder and first president of the Jefferson Society of Clinical Investigation; in 1941 received a certificate of merit from the American Medical Association for an exhibit on infusions of blood and other fluids into the circulation via the bone marrow; veteran of World War I; a member of the board of corporators of the Peddie School in Hightstown; served as director of the Charlotte Drake Cardeza Foundation and Laboratories of the division of hematology at Jefferson Medical College; died Sept. 2, aged 68.

Jones, Ransom Julaney Ⓜ Kinston, N. C.; Emory University School of Medicine, Atlanta, 1932; health officer of Lenoir and Jones counties; veteran of World War II; died Aug. 20, aged 51.

Kimbrough, Charles Talmage, New York City; Syracuse University College of Medicine, 1925; veteran of World War I; died in the Veterans Administration Hospital Aug. 14, aged 65.

Lewis, Michael, Georgetown, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1938; for many years associated with the Baldpate Hospital; died in Portsmouth, N. H., Sept. 1, aged 51.

Lippman, Louis Simeon Ⓜ Chicago; Chicago College of Medicine and Surgery, 1911; died Sept. 1, aged 79.

McLaughlin, Ralph Lenard Ⓜ San Antonio, Texas; University of Louisville (Ky.) School of Medicine, 1917; served with the U. S. Veterans Administration; veteran of World War I; died in the Scott and White Memorial Hospital in Temple June 5, aged 67.

Mixson, Harold Joyce Ⓜ Beaumont, Texas; Tulane University School of Medicine, New Orleans, 1921; at one time associated with the South Mississippi Charity Hospital in Laurel; died in the Baptist Hospital of Southeast Texas Aug. 29, aged 64.

Mundell, Joseph Joshua Ⓜ Washington, D. C.; born in Anacostia Dec. 22, 1879; Georgetown University School of Medicine, Washington, 1903; specialist certified by the American Board of Obstetrics and Gynecology; fellow of the American College of Surgeons; resigned from the regular Navy on Feb. 6, 1942; professor of obstetrics from 1934 to 1947, when he became professor of obstetrics emeritus at his alma mater; charter member and past-president of the Washington Gynecological Society; helped found the Georgetown Clinical Society, which in 1945 presented him with its first G award for distinguished service in the practice of medicine or surgery; consultant to the U. S. Naval Hospital in Bethesda; associated with the Providence Hospital, Georgetown Hospital, and Columbia Hospital for Women; died at Ocean City, Md., Aug. 30, aged 79.

North, Frank Raymond Ⓜ Winfield, Iowa; Keokuk (Iowa) Medical College, College of Physicians and Surgeons, 1904; past-president of the Henry County Medical Society; died in Muscatine Aug. 15, aged 83.

Oakley, E. Reed Ⓜ Pasadena, Calif.; University of Nebraska College of Medicine, Omaha, 1932; also a graduate in pharmacy; interned at the University of Nebraska Hospital in Omaha; formerly practiced in Lincoln, Nebr.; died Aug. 20, aged 60.

Otto, Harold Lese, New York City; University and Bellevue Hospital Medical College, New York City, 1920; associated with the Beth Israel Hospital and the Hospital for Joint Diseases; died in Saratoga Springs, N. Y., Sept. 9, aged 65.

Powers, Edward Parnell Ⓜ Boston; Georgetown University School of Medicine, Washington, D. C., 1905; associated with the Milton (Mass.) Hospital, New England Hospital, and the Parker Hill Medical Center; died Sept. 2, aged 78.

Pratt, George Olin Ⓜ Alburg, Vt.; born in Enosburg Falls, June 5, 1910; University of Vermont College of Medicine, Burlington, 1935; interned at the Bishop De Goesbriand Hospital in Burlington; during World War II served overseas in the European Theater as commanding officer of the 70th Station Hospital, during which time he received numerous commendations and decorations; in 1946 discharged from Army with the rank of colonel; member of the Association of Military Surgeons of the United States and the Reserve Officers Association; became associated with the Veterans Administration and after a short time in the Shreveport, La., regional office became manager of the Veterans Administration Hospital in Amarillo, Texas; later became assistant director of the New England–New York area of the Veterans Administration; served as manager of the Veterans Administration hospitals in Manchester, N. H., Brooklyn, and Syracuse, N. Y.; in 1956 established the Pratt Clinic in Alburg, serving as director as well as county medical examiner and health officer; associated with the Kerbs Memorial Hospital and St. Albans Hospital in St. Albans; a member of Rotary Club; died Aug. 26, aged 49.

Quirk, William Ambrose, Evergreen, La.; Louisville (Ky.) Medical College, 1889; died July 18, aged 93.

Randall, Joseph Alexander Ⓜ Harrisburg, Pa.; Howard University College of Medicine, Washington, D. C., 1931; civilian chief of occupational medicine at the Olmsted Air Force Base in Middletown, where he died Sept. 2, aged 54.

Reetz, Frederick August Ⓜ Shelby, Mich.; the Hahnemann Medical College and Hospital, Chicago, 1905; at one time practiced in Muskegon, Mich., where he was on the staff of the Hackley Hospital; on the staff of the Shelby Community Hospital; died Aug. 17, aged 76.

Richmond, James, Coquille, Ore.; Saginaw (Mich.) Valley Medical College, 1902; died in Myrtle Point Sept. 2, aged 85.

Robbins, Noel Walker, Delray Beach, Fla.; Duke University School of Medicine, Durham, N. C., 1932; interned at the Duke Hospital in Durham, N. C., and the Charlotte Memorial Hospital in Charlotte, N. C.; died in the Bethesda Hospital in Boynton Beach July 18, aged 51.

Rosenthal, Jacob Sontheimer, Washington, D. C.; Tulane University School of Medicine, New Orleans, 1915; veteran of World War I; died near Sweetwater, Tenn., Sept. 5, aged 65.

Rutledge, John Richard, Greenwich, N. Y.; University of Rochester School of Medicine and Dentistry, Rochester, N. Y., 1958; interned at the Bellevue Hospital Center in New York City; captain in the U. S. Air Force; died Aug. 25, aged 27.

Saville, John William, Bethesda, Md.; George Washington University School of Medicine, Washington, D. C., 1953; formerly served in the U. S. Naval Reserve; interned at the Naval Hospital in Bethesda, Md.; served a residency at the Bellevue Hospital Center in New York City and the Massachusetts General Hospital and the Children's Medical Center in Boston; orthopedic resident at the District of Columbia General Hospital in Washington, D. C.; certified by the National Board of Medical Examiners; died in Annapolis, Md., Sept. 12, aged 30.

Shapiro, Julius Robert, Belle Harbor, N. Y.; University of Dublin School of Physics, Trinity College, Dublin, Ireland, 1935; interned at Jersey City Hospital in Jersey City, N. J., and Hudson County Tuberculosis Hospital and Sanatorium in Secaucus, N. J.; served a residency at the Boulevard Hospital, Long Island City, N. Y., and the Brooklyn Eye and Ear Hospital in Brooklyn; died in the Beth Israel Hospital in New York City Aug. 23, aged 49.

Smith, Millicent Zenos Ⓜ Palo Alto, Calif.; Baylor University College of Medicine, Dallas, 1941; interned at Santa Clara County Hospital in San Jose, Calif.; veteran of World War II; member of the American Academy of General Practice; died Aug. 30, aged 46.

Studer, Adolph Gustav, Grosse Pointe, Mich.; Detroit Homeopathic College, 1903; retired general secretary of the Detroit YMCA; died in the Bon Secours Hospital Aug. 16, aged 91.

Taylor, George Mosser Ⓜ Los Angeles; College of Medical Evangelists, Loma Linda and Los Angeles, 1924; certified by the National Board of Medical Examiners; specialist certified by the American Board of Orthopaedic Surgery, Inc.; member of the American Academy of Orthopaedic Surgeons; fellow of the International College of Surgeons; professor and chairman of the department of orthopedic surgery at his alma mater; on the senior attending staff of the Los Angeles County Hospital and the White Memorial Hospital; died Sept. 1, aged 61.

Taylor, H. Williams Ⓜ Little Compton, R. I.; born in 1886; Columbia University College of Physicians and Surgeons, New York City, 1915; fellow of the American College of Surgeons; served as member and chairman of the Little Compton school committee and as medical examiner; a staff surgeon at St. Anne's Hospital in Fall River, Mass.; on the courtesy staffs of the Truesdale and Union hospitals of Fall River, Mass., and St. Luke's Hospital in New Bedford, Mass.; at one time practiced in Englewood, N. J., where he was associated with the Englewood Hospital; died Sept. 7, aged 72.

Theriault, Louis Leo Ⓜ Wethersfield, Conn.; Jefferson Medical College of Philadelphia, 1918; died Aug. 30, aged 66.

Thomas, Edward Philip Ⓜ Frederick, Md.; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1916; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons; past-president of the Medical and Chirurgical Faculty of Maryland and the Frederick County Medical Society; past-president of the state board of medical examiners; veteran of World War I; associated with the Frederick Memorial Hospital; died Aug. 25, aged 67.

Timm, John A., Brooklyn; University of Minnesota Medical School, Minneapolis, 1919; fellow of the American College of Surgeons; veteran of World War I; served on the staffs of the Kingston Avenue, Methodist, and Cumberland hospitals; died in Altura, Minn., July 22, aged 69.

Toller, Else Ⓜ New York City; Ludwig-Maximilians-Universität Medizinische Fakultät, München, Bavaria, Germany, 1919; interned at the Bronx Hospital in New York City; served a residency at the Overlook Hospital in Summit, N. J., and the Craig House in Beacon, N. Y.; associated with the U. S. Veterans Administration; died in the Flower and Fifth Avenue Hospitals Aug. 5, aged 66.

Tomb, Andrew Spencer Jr. Ⓜ Victoria, Texas; Tulane University School of Medicine, New Orleans, 1933; served as vice-president of the Texas Medical Association; past-president of the Texas Academy of General Practice and the Victoria-Goliad-Calhoun Counties Medical Society; past-president of the Victoria Independent School Board; member of the American Academy of General Practice and the Industrial Medical Association; died in Shreveport, La., Aug. 26, aged 48.

Torrence, Allen Coutler, Hot Springs National Park, Ark.; Meharry Medical College, Nashville, Tenn., 1912; died in the Quachita General Hospital Aug. 15, aged 70.

Vinson, Porter Paisley Ⓜ Richmond, Va.; born in Davidson, N. C., Jan. 24, 1890; University of Maryland School of Medicine, Baltimore, 1914; specialist certified by the American Board of Internal Medicine; member of the Southern Medical Association, American Broncho-Esophagological Association, American Association for Thoracic Surgery, Alumni Association of the Mayo Foundation, of which he was president in 1940, Society of the Sigma Xi, Phi Beta Kappa, and the Nu Sigma Nu professional medical fraternity; fellow of the American College of Physicians; professor of bronchoscopy, esophagoscopy, and gastroscopy at the Medical College of Virginia; formerly associated with the Mayo Clinic and Mayo Foundation, Graduate School, University of Minnesota, in Rochester, Minn.; veteran of World War I; on Dec. 12, 1939, delivered the thirteenth annual Dr. Stafford E. Chaille Oration of the Orleans Parish Medical Society in New Orleans; in 1925 the Davidson College in Davidson, N. C., awarded him the honorary degree of doctor of science; died in St. Mary's Hospital, Rochester, Minn., Aug. 28, aged 69.

Watson, Walter Hunter, Greenville, S. C.; Medical College of South Carolina, Charleston, 1939; interned at the Roper Hospital in Charleston; veteran of World War II; associated with the Greenville General Hospital and the St. Francis Hospital, where he served a residency, and where he died Aug. 15, aged 44.

Weinreb, William Aron Ⓜ Brooklyn; Medizinische Fakultät der Universität, Vienna, Austria, 1923; member of the American Academy of General Practice; died in the Jewish Hospital Aug. 23, aged 68.

Zibel, Nathan, Quincy, Mass.; Tufts College Medical School, Boston, 1926; associated with the Brookline (Mass.) Hospital, South Shore Hospital, Weymouth, and the Quincy City Hospital; died in the Bournewood Hospital, Brookline, Aug. 28, aged 56.

FOREIGN LETTERS

BRAZIL

Intestinal Parasitosis.—Wolffenbuttel and Zelmanowicz (*Journal of the Medical Association of Rio Grande do Sul*, June, 1959) evaluated the treatment of several intestinal parasitoses by new drugs. They summarized their findings as follows: Oxytetracycline was preferred for amebiasis. Giardiasis was treated successfully with a combination of chlorquinaldol, chlorbetamide, and quinacrine. In pinworm infection good results were obtained with piperazine and optional results were obtained with dithiazanine. No completely satisfactory treatment for ascariasis or whipworms was found. Hexylresorcinol in doses of 1 Gm. daily for 5 to 10 days proved effective in the treatment of hookworm. Dithiazanine given in increasing doses (100 mg. on the 1st day, 200 on the 2nd, 300 on the 3rd, and 400 on the 4th to the 10th day) is the drug of choice in the treatment of strongyloidiasis. In the treatment of tapeworms quinacrine administered by duodenal tube was preferred.

CHILE

Scleroderma.—A. Gonzalez Salvatierra (*Rev. méd. Chile* 87:498, 1959) treated a series of 17 patients who had scleroderma with cortisone or prednisone over a period of one to three years. The results were excellent in eight, good in six, fair in one, and poor in two. In some combining steroid treatment with chloroquine improved the results and made it possible to lower the dosage of cortisone.

Iproniazid and Hepatitis.—Katz and Ducci (*Rev. méd. Chile* 87:421, 1959) treated a series of 69 patients (48 who had psychiatric disorders and 21 who had angina pectoris) with iproniazid. Both groups were given an initial dose of 100 to 150 mg. daily, and a maintenance dose of 25 to 100 mg. daily. The psychiatric group was treated for an average of 90 days and the cardiac group for an average of 65 days. Only one patient developed hepatitis and this was a viral type. The authors concluded that iproniazid is not hepatotoxic and if hepatitis develops while it is being given some other explanation should be sought.

Splenoportography.—C. Larrain (*Rev. méd. Chile* 87:410, 1959) performed percutaneous splenoportography on 56 patients, most of whom had cirrhosis of the liver, and obtained positive results in 49. Roentgenograms were made three, six, and nine seconds after injection of the contrast medium. Side-effects (nausea and flushing) appeared in only 10 patients. This procedure proved to be useful in differentiating intrahepatic and extrahepatic portal hypertension and in the diagnosis of the hydatid disease and malignant metastases in the liver.

FRANCE

Exophthalmic Goiter.—At the meeting of the National Academy of Medicine, on Jan. 20, De Gennes reported success with radioiodine (I^{131}) in 90% of 800 patients with exophthalmic goiter. The initial dose proved to be insufficient in 20% of the patients, and they were given another dose a few weeks later. There was no improvement in 3% of the patients.

De Gennes and co-workers (*Semaine des Hôpitaux*, April 28, 1959) reported a series of 138 outpatients with hyperthyroidism who were given I^{131} intravenously in amounts producing about 10,000 rads. Patients in whom signs of progressive hyperthyroidism persisted were given another dose three months later. All the patients in this series had progressive hyperthyroidism and had failed to respond to medical treatment. The follow-up period of 18 months showed that in 79% of the patients the thyroid state returned to normal and the cardiovascular, neurovegetative, and metabolic manifestations disappeared and the body weight returned to normal. In 16% of the patients permanent postoperative hyperthyroidism was noted. The treatment failures in 1.4% and the incomplete cures in 3.6% of the patients were attributable to the atypical characteristics of the disease, and to the relatively moderate uptake of I^{131}. Of 109 patients whose thyroid state returned to normal 60 (55%) had no return of symptoms. Of the remaining 49, exophthalmos returned in 37, goiter returned in 12, and auricular fibrillation returned in 7. The basal metabolic rate (BMR) returned to normal in almost all of the patients whose thyroid state returned to normal without sequelae. The BMR never exceeded 30% in the patients who were cured but who had a return of symptoms. None of the patients developed thyroid cancer, radiation sickness, or hematological disorders. The patients with severe exophthalmos were better able to tolerate large doses of I^{131} than those with mild exophthalmos, and those with cardiac insufficiency or auricular fibrillation had a high tolerance for the drug.

The items in these letters are contributed by regular correspondents in the various foreign countries.

Hyperthyroidism.—At the meeting of the Academy of Surgery, H. Welti reported a series of 12,000 thyroidectomies which he performed in a period of 30 years. In this series 7,000 had hyperthyroidism, which in most of the patients was severe. They were medically treated before the operation for months or years without success. The operative mortality was only 0.2% despite the severity of the condition in some of the patients. A review of the 6,619 thyroidectomies performed between January, 1951, and October, 1955, revealed that of the 3,371 patients subjected to thyroidectomy because of exophthalmic goiter 8 died, and of the 2,958 who were operated on for simple goiter 5 died.

The great advantage of thyroidectomy over treatment with I^{131} consists, according to the author, in the complete or almost complete cure of the hypothyroidism. In some patients complete cure occurred within a few weeks, and in others even within a few days. In most patients the exophthalmos disappeared promptly. On the other hand, the action of I^{131} is slow and in many patients disappointing. In some patients a severe and persistent myxedema develops after treatment with I^{131}, particularly in patients with exophthalmos aggravated by hypophysial involvement. This thyroid insufficiency is especially unfortunate in older persons who are predisposed to arteriosclerosis by the resulting increase in their cholesterol level. The effect on the gonads is a reason to avoid this treatment in young persons. Treatment with I^{131} is especially contraindicated in children and pregnant women. The author called attention to the fact that thyroidectomies performed after treatment with I^{131} has failed are often technically difficult because the goiters are difficult to exteriorize, they are easily torn, they bleed profusely, and great care is needed to protect the recurrent laryngeal nerves and the parathyroids.

GERMANY

X-ray Contrast Mediums Containing Iodine.—E. Schulte (*Medizinische,* no. 17, page 839, 1959) reported that the number of x-ray examinations with iodine-containing contrast mediums has increased in recent years. Numerous complications following the use of such mediums have been reported in Sweden and America. The author made 6,000 intravenous urographies and 200 venographies in the past 10 years. In this series he observed allergic skin reactions with reddening of the skin, itching, urticaria, and edema in only three patients. These side-effects were successfully treated with antihistaminics. Prior to the examinations with the contrast mediums, some drops of the agent to be used were instilled into the patients' conjunctivas. Since these tests were negative even in the patients who later showed allergic reactions, it was of no prognostic value. With every contrast demonstration with mediums containing iodine it is, however, necessary that a sterile syringe and antihistaminics be kept at hand to remedy any allergic reactions at once. Even with slow injections patients complain sometimes of hot flushes, dizziness, and nausea. In some, vomiting may occur. These reactions subside completely after a few minutes.

Iodipamide used for 2,500 cholecystograms was well tolerated. A severe collapse with generalized exanthema was observed in one patient after a dose of only 1.5 cc. With intra-arterial administration of the contrast agents the author knew of 300 such cases. Side-effects occurred more frequently and were more severe than when intravenous injections were given. Prior to every injection the cardiac, circulatory, and renal function should be examined. With cerebral angiographies hemiplegia occurred in one patient but disappeared completely after two days. Allergic reactions were seen in two arteriographies. A severe complication occurred in a woman with peripheral circulatory disorders in the lower extremities, after a total of 120 cc. of a contrast agent had been given. The patient suffered an anaphylactic shock, anuria, and nephrotic changes. It is recommended that, if possible, not more than 60 cc. of a contrast medium containing iodine be given at a time.

Nicotine and Circulatory Diseases.—F. Lickint (*Landarzt* 35:470, 1959) reported on experimental investigations which showed that while smoking one cigarette about 1.6 mg. of nicotine is taken up by the lungs. The amount of the nicotine reaching the blood stream is sufficient to produce the typical effects on the circulation. The effect of nicotine on the capillaries can be observed on the nail-groove. The capillaries are constricted and partly even occluded, which results in stasis. Not all parts of the body respond in the same manner. This phenomenon is not seen, for instance, in the ears. A marked fall of temperature is produced at the peak of the capillary constriction. This begins after about 10 minutes and reaches the lowest value after 30 minutes. After 60 minutes the normal temperature is restored. The average drop of temperature is between 2.5 and 3.2 C. A constriction of the arterioles is also observed. This can best be demonstrated by the time required for the rewarming of the fingers after a five-minute handbath in water at 15 C. This time of rewarming is lengthened by smoking a single cigarette, and lasts one hour instead of only five minutes.

Dr. Güth demonstrated that the rewarming of the skin (normally achieved after massage) is completely missing if the patients smoke a cigarette during treatment. It was shown in animal experiments with contrast agents that the arteries contracted like a string of pearls when nicotine was given. Follow-up examinations in patients suffering from vascular diseases, in whom vascular transplantation had to be performed, showed that the restoration of the normal blood supply could be achieved only in nonsmokers. Cigarette smoking also played a great part in the healing process of frostbite in World War II. Alterations of coronary vessels could be produced experimentally in animals by regular administration of nicotine. These findings are in agreement with clinical experiences. Myocardial infarction occurs much more frequently in smokers than in nonsmokers. In these cases, hormonal factors also seem to play a part. The nicotine probably eliminates the vasopressin of the posterior lobe of the hypophysis, which, in turn, produces vasoconstriction and inhibition of diuresis.

Embryonal Carcinosarcoma.—P. Kolle (*Deutsche med. Wchnschr.* 84:1287, 1959) stated that the prognosis in children with sarcoma of the kidneys is better than previously. Operation and immediate subsequent irradiation is the method of choice. Patients with nephroblastoma should be operated on four or five hours after admission. Any further delay may worsen the prognosis. Undue palpation may result in dissemination of tumor cells; therefore, examination should be performed once only and as carefully as possible. Less experienced surgeons should choose preliminary irradiation, since a marked involution of the tumor is usually achieved by this measure. In consequence tearing of the tumor during operation occurs less frequently, and the tumor cells do not get into the blood stream so easily by manipulations. An optimal result can only be obtained if children with nephroblastoma are treated in suitable clinics. The decisive factor, however, is the early diagnosis.

Pulmonary Embolism.—Böwing and Thedering (*Landarzt* 35:464, 1959) reported that pulmonary embolism was found to be the cause of death in about 3% of autopsies. Thrombosis is found mostly in the region of the inferior vena cava, whereas thromboses in the region of the superior vena cava are very rare. Patients with pulmonary embolism do not always take the same course. Only 18% died within the first 24 hours, 42% in one to seven days, and 40% after seven days. These figures show that proper therapy of pulmonary embolism is possible in most patients. Pulmonary embolism occurs more frequently in women than in men. Massive embolism of the main trunk or of one of the two main branches of the pulmonary artery leads to sudden death, but in most patients only the smaller arteries are affected. Death is probably due to an acute strain of the right heart, as a result of which collapse of the systemic circulation with cerebral anoxemia and coronary insufficiency may occur; 75% of the patients complain of severe chest pain.

Here a distinction must be made between the first phase of pain, due to the excessive dilatation of the pulmonary vessels, and the second or late phase of the pain. The latter is caused by the accompanying pleurisy. Besides the pain there is often a collapse with severe dyspnea associated with anxiety and blood-stained sputum, especially when congestion of the pulmonary circulation was already present. General vegetative symptoms, such as fever, leukocytosis with a shift to the left and eosinopenia, accelerated sedimentation rate, and a shift in the region of serum albumin occur after some hours. Roentgenographic findings are recognizable only after 24 hours, mostly in the form of round shadows or atelectasis. Electrocardiograms reveal cor pulmonale, sometimes incomplete right heart block, and more or less defined alterations of the final ventricular deflections. The findings may suggest pulmonary infarction, pericarditis, pleurisy, or acute abdominal disease. The first therapeutic measures are to care for the dilatation of the bronchial arteries, to combat the shock, and to prevent further embolic complications. The drugs to be given are papaverine, a papaverine homolog (Eupaverine), theophylline preparations, and morphine for the relief of pain.

In severe embolism with shock, the shock should be treated first since in this state patients are not transportable. Circulatory stimulants and digitalis preparations should also be given. In order to prevent further embolism it is necessary to administer heparin. The doses should be large enough to reduce the risk of further embolism. Heparin is at first injected every six hours. On the second or third day a change to bishydroxycoumarin should be made. Careful checks of the bleeding time are indispensable. If hemorrhages do occur while heparin is being given, protamine sulfate may be used as an antidote, and when hemorrhages occur while bishydroxycoumarin is being given, vitamin K is the preferred antidote. Special care should be taken with anticoagulants in the presence of liver diseases. Allergic reactions may occur with heparin preparations which necessitate a change to another preparation.

γ-globulins for Hepatitis.—H. Mittelmeier of the Free University of Berlin (*München. med. Wchnschr.* 101:1450, 1959) reported on the treatment of viral hepatitis, an epidemic of which developed in an orthopedic ward. The epidemic lasted for about six months during which six children and five members of the hospital staff became victims. The serial immunization of the department with γ-globulins given in two doses of 0.02 ml. per kilogram of body weight, at intervals of two to three weeks, resulted in cessation of the epidemic.

Seborrheic Dermatitis.—G. Wolfram (*München. med. Wchnschr.* 101:1398, 1959) reported a series of 85 infants admitted to the hospital with seborrheic dermatitis who were given injections of vitamin B_{12} in a dosage of 15 to 30 mcg. weekly and appropriate nourishment. A bland ointment was applied locally. In each case all skin lesions were cured within 18 to 21 days and the concomitant anemia was improved.

Spiramycin.—G. Muhlhardt (*Deutsche med. Wchnschr.* 84:1545, 1959) used spiramycin in the treatment of gram-positive and gram-negative infections in 60 patients (33 with local abscesses or carbuncles, 14 with osteomyelitis, 8 with cholangitis, 4 with pleural empyema, lung abscess or pneumonia, and 1 with enterocolitis). Good results were obtained in 52 patients. Most of the infections were due to hemolytic Staphylococcus aureus. The drug was well tolerated and without significant side-effects. The following indications proved reliable: (1) infections with organisms resistant to the common antibiotics, (2) osteomyelitis, and (3) biliary tract infections because the drug is concentrated in bile.

Vitamin K Treatment in Neonates.—Synthetic vitamin K given by J. Ströder and co-workers of Würzburg (*Deutsche med. Wchnschr.* 84:1553, 1959) in doses of 10 mg. intramuscularly or 30 mg. by mouth proved effective and produced no side-effects when given to a large number of full-term and premature newborn infants. Vitamin K_1 however was found to be even more effective, 1 mg. intramuscularly being a fully effective dose. It achieved complete and rapid reversal of all clotting deficiencies caused by a lack of vitamin K in the premature infants.

Detoxication with Polyvinylpyrrolidone.—As a result of many years of experience with a 6% isotonic solution of polyvinylpyrrolidone (PVP) having a mean molecular weight of 12,600, H. Sikorski of Kaiserslautern (*Clinical Excerpts,* vol. 4, 1959) considered the preparation valuable for effecting detoxication and combating dehydration. It proved its value, for example, in 359 patients with burns, mostly severe. After a loss of 300 to 500 cc. of blood or serum up to 1,000 cc. of PVP solution was infused at a rate of 100 cc. in 10 to 15 minutes. When it was possible to make the infusion shortly after the accident, the primary shock was always prevented. Combined local dressings and PVP solution also prevented the development of keloids.

In radiation sickness, subjective symptoms usually disappeared after the third injection of 50 cc. of PVP solution, given daily in combination with vitamins and dextrose. The severe symptoms of acute allergic toxicodermas, with edema of the face and extremities, were also greatly benefited by drip infusions or three daily injections of 100 cc. of PVP solution. Patients with oliguria after poisoning with heavy metals and others with cerebral edema resulting from administration of the arsphenamines were also successfully treated with PVP. Liver damage subsequent to arsphenamine treatment improved under simultaneous liver therapy and PVP treatment in a short time and was completely cured within a few months. Herpes gestationis in 21 women disappeared after combined treatment with 10 cc. of PVP solution plus a carbonase inhibitor and promethazine. In 37 patients with endarteritis obliterans and thromboangiitis obliterans in whom treatment with vasoactive drugs and bed rest had been unavailing daily injections of PVP solution (in some patients up to 300 cc.) caused the pain to subside after a short time. The affected areas cleared and the necrotic distal parts showed distinct demarcation.

INDIA

Anticoagulant Therapy.—R. N. Chakravarti and co-workers (*Indian Journal of Medical Sciences,* vol. 13, July, 1959) stated that drugs of the heparin type have been found to be effective against cardiovascular thromboembolic diseases, which, in most cases, are associated with atherosclerosis. They studied another type of anticoagulant, ethyl-biscoumacetate (Tromexan), in chicks with experimentally produced atherosclerosis. The animals were divided into four groups. The first group was fed plain mash; the second received a mash containing 0.5% cholesterol; the third received, in addition to cholesterol, 1 mg. of Tromexan; and the last group was kept on mash supplemented by 1 mg. of Tromexan without cholesterol. The chicks were killed at intervals of 4, 8, and 12 weeks and the gross and microscopic cardiovascular changes were studied.

The first and fourth groups did not show any atheroma. Animals in the second group showed a gradual increase in size of atheromatous plaques in proportion to the duration of feeding of cholesterol. At all stages of development the lesions in the thoracic aorta were much more advanced than those in the abdominal aorta. Microscopically, the earliest change was an aggregation of foam cells in the intima. There was also proliferation of intimal reticulin and collagen possibly due to increased imbibition and deposition of lipids in the intima. The chicks in the third group also developed plaques but their size at various periods of feeding, in both thoracic and abdominal aorta, was smaller than that of group 2.

Tromexan did not enhance the severity of the lesions. The apparent inhibition produced by Tromexan as shown by the smaller size of lesion in chicks receiving cholesterol and Tromexan as compared to those receiving cholesterol alone was probably due to its antagonizing of prothrombin leading to a lowered blood thrombin content. Tromexan given alone did not produce any atheromatous changes. The difference in size of the plaques in the thoracic and abdominal aorta at same periods of feeding may have been due to the action of structural and biochemical tissue factors which are present in the vessel wall and are important in the presence of altered serum composition in the development of these lesions and are also responsible for the difference in intensity and extent of atherosclerosis in different arterial trees.

The effect of Tromexan was also studied on serum lipids, proteins, and lipoproteins in experimental atherosclerosis of chicks. Marked biochemical changes were noted at different periods in the serum of these animals. Cholesterol feeding was associated with marked hypercholesteremia. Those animals receiving cholesterol showed hyperglobulinemia of the alpha-2 and beta fractions with beta lipoproteinemia. Administration of Tromexan for 12 weeks caused a slight increase in serum total cholesterol and lipid phosphorus and lowered the free cholesterol level. At 4 weeks, alpha-2 and beta globulins were reduced but at 12 weeks of drug feeding, the alpha-2 fraction was increased and the alpha/beta lipoprotein ratio showed an increase due to a relative increase in alpha lipoprotein. The increase in total cholesterol after cholesterol feeding was not prevented by Tromexan, but the level of free cholesterol was lowered with a rise of the ester fraction. The beta globulin level showed relative reduction in cholesterol-fed chicks who were given Tromexan while continued feeding of the drug raised the alpha-2 globulin level. The increase in alpha/beta lipoprotein ratio may have been due to stimulation of the active factor, lipoprotein lipase. This action is similar to the action of heparin.

Coronary Artery Disease and Cor Pulmonale.—R. M. Kasliwal and co-workers (*Indian Journal of Medical Sciences*, vol. 13, July, 1959) stated that they frequently observed patients with cor pulmonale co-existing with coronary heart disease in the form of ischemia, bundle-branch block, or myocardial infarction. These lesions were detected on routine ECG's. They were painless from the start and the patients were unaware of the cardiac damage. No history of chest pain could be elicited. A mild degree of systemic hypertension was frequently observed in patients with severe cor pulmonale. The authors reported a series of six selected patients with cor pulmonale who had electrocardiographic evidence of coronary disease. Three of these showed myocardial infarction, one showed left bundle-branch block, one showed myocardial ischemia, and one had evidence of left ventricular hypertrophy and strain.

Although coronary artery disease and cor pulmonale occur in the same age group, the two are believed to be of independent origin by some authors, but the anoxia produced by the presence of cor pulmonale is likely to aggravate the coronary lesion. There is also diminished blood flow through the coronary vessels, which increases the anoxia and leads to coronary artery disease. Clinically these cases are difficult to diagnose because of the absence of pain. Electrocardiographic findings are helpful but they can also be confusing; only autopsy reveals the full damage particularly in a patient with cor pulmonale whose dyspnea is out of proportion to the extent of his pulmonary lesions.

Plasma Protein Levels of Healthy Medical Students.—Best and Vaidya (*Indian Journal of Medical Sciences*, vol. 13, July, 1959) estimated the plasma protein levels in 70 students (55 men and 15 women) between 18 and 23 years of age. The blood samples were collected within two hours after breakfast. All the students were in good nutritional status. Most of them were used to a vegetarian diet and those who were nonvegetarians took meat only occasionally. About 8 oz. of milk was consumed daily by all. No significant difference in the levels of plasma proteins was detected due to diet. The total plasma proteins in the men averaged 7.11 Gm. per 100 ml. In the women it averaged 6.94 Gm. per 100 ml. The mean albumin concentration for the men was 4.20 Gm. per 100 ml. and for the women 4.0 Gm. per 100 ml. The values for mean total globulin were 2.99 Gm. per 100 ml. in the men and 2.87 Gm. per 100 ml. in the women. The values for albumin for both sexes were a little lower and those for globulin a little higher than those obtained by other workers.

Pulmonary Arteriosclerosis.—R. K. Goyal and co-workers (*Indian Journal of Medical Sciences*, vol. 13, July, 1959) stated that a high incidence of emphysema and consequent cor pulmonale has been reported in a northern state of India while others found much pneumoconiosis in the nonindustrial population from the same area. As lesions of pulmonary vessels are often associated with cor pulmonale, the authors studied lungs from 127 autopsies and examined 152 pulmonary arterioles with variable lesions. Marked intimal thickening was found in 17, medium in 33, and slight in 29 vessels. Five showed thrombosis with recanalization. Thickening of adventitia and intima was associated with moderate carbon pigmentation in 10, moderate medial thickening in 27, and slight medial thickening in 2 vessels. Both intima and media were thickened in 13 vessels, 9 showed atheroma, 2 had evidence of arteritis, and 5 had no thickening.

Thus, a large percentage showed thickening of the vessel wall and the lesions could be classified as (1) those due to pulmonary hypertension; (2) those produced by pulmonary hypertension and abnormal proliferation of intimal fibrous tissue; and (3) endarteritis obliterans. This material came from autopsies of persons who had had a wide variety of such unrelated diseases as cirrhosis, nephritis, and malignancy, but an overwhelming majority had varying degrees of pulmonary lesions in the form of interstitial pneumonitis, emphysema, chronic venous congestion, fibrosis, and edema which were probably responsible for the changes in the walls of pulmonary vessels. Experimental confirmation was sought by intrapulmonary injection of dust into guinea pigs who developed definite thickening of some of the pulmonary arterioles after three months Similar results were obtained with intraperitoneal injection of local dust and silicon dioxide, a larger number of vessels being affected when the number of injections was increased.

In rabbits a single large dose injected into the lung caused thrombosis and a smaller number of injections of dust led to moderate thickening of the vessels. Inhalation of dust for varying periods also produced changes in vessel walls in rabbits and guinea pigs. The animals were made to inhale finely powdered wood charcoal as the urban population has to inhale a lot of carbon particles. Similar vascular changes were produced after about 26 days of inhalation. Inhalation of a mixture of dust and charcoal caused marked thickening. Intrapulmonary and intraperitoneal injections of silicon dioxide led to arteriolar necrosis and thrombosis in most of the rabbits subjected to these injections. To study the action of infective agents on the arteriolar walls, sublethal injections of Escherichia coli were given intraperitoneally when no thickening of pulmonary vessels was noticed, while a few arterioles were found thickened after intraperitoneal and intramuscular injections of tubercle bacilli. The important cause of cor pulmonale in the cases studied was inhalation of dust leading to medial muscular hypertrophy which in turn led to pulmonary hypertension.

Mammary Carcinoma.—Ghooi and Nigam studied the value of several tests in the diagnosis of early and doubtful cases of mammary carcinoma (*Antiseptic*, vol. 56, July, 1959). Bolen's test, based on the differences in appearance of a drop of blood allowed to dry on a slide and examined grossly and microscopically, was done in 50 patients and gave a positive finding in 40, a negative finding in 6, and a doubtful reading in 4. False-positive results were obtained in patients with liver disease and during pregnancy. Tangential roentgenography of the breast in the lateral or tangential plane showed distinctive appearances for carcinoma, benign tumors, and tuberculosis of the breast. Lipiodol and air mastography were also done in some patients but the latter was found to be too unpleasant and not very helpful.

Discharge from the nipple showed epithelial cells with retained secretions normally, while cloudy serum was obtained in duct-epithelium or papillary disease. Blood stained discharge suggested carcinoma, adenoma, or papilliferous cystic disease. Hemograms were studied in 130 patients. In 30 the total red blood cell count and hemoglobin percentage were within normal limits and 100 had some degree of anemia. The total leukocyte count was normal in 60 patients, slightly increased in 30, slightly lowered in 30, and markedly altered (the count being below 3,000 or over 25,000) in 10. The differential count showed relative eosinopenia although the lymphocytes were unaltered. The sedimentation rate, measured in 50 patients, was normal in 14, raised in 33, and subnormal in 3. Of the entire series 60% belonged to blood group B, although this constituted only 9% of the total population. The serum calcium level was raised in most patients who had osseous metastases. It showed a transient tendency to decrease in six patients treated with hormones, while hypercalcemia was an index of progression of the metastases.

Liver function tests showed a slight derangement in some patients without hepatic insufficiency. They served as a reliable index of liver involvement and in the assessment of the progression of the lesion. In four advanced cases repetition of liver function tests after three weeks of hormonal treatment showed a short-lived regression. Sternal puncture done in 40 patients was positive for malignant cells in 10. The type of primary growth did not determine the sternal metastases nor did the absence of such a spread exclude the presence of metastases elsewhere. Tissue fluid from a cancer mass showed a high protein content but no organisms or inflammatory reaction to account for this and suggested a high catabolic activity on the part of the tumor cells.

Nonoperative Treatment of Femoral Fractures.—Ohri and Hatim got excellent results with nonoperative treatment for trochanteric fractures with a case fatality rate of only 2% (*Indian Journal of Surgery*, vol. 21, June, 1959). In a series of 50 consecutive cases, they found that it was most common in the group aged 51 to 60 years, although their youngest patient was 18 and the oldest 100 years of age. Men predominated in the younger age group and women in the older. Trivial trauma accounted for 33 fractures and severe trauma accounted for the rest. Twenty-nine patients were treated by skeletal traction in a Bohler splint, eight by skin traction in a Bohler splint, five by skeletal Russell traction, and six by skin Russell traction, and two had not received any treatment but came to the hospital when their fractures had already united in malposition. Only one death (from bronchopneumonia) occurred during treatment. Of the survivors 29 had a normal gait, 10 had a mild limp, and 10 had a moderate limp after treatment; 48 had no pain and one complained of mild pain without any interference with activity or function.

Full range of movement was restored in 37 and the rest had a fair range of movements at the hip. The knee movements were full in 47 patients and fair in 2. There was no shortening of the limb in 32, a shortening of less than 1 in. in 11, and of 1 in. or more in 6. All the patients treated by skeletal Russell traction obtained excellent results. Their fractures healed in an anatomic position with full painless range of movement and the patients were able to walk without support. Only 78.6% and 62.5%, respectively, of those treated by skeletal and skin traction in a Bohler splint obtained excellent results. None of the patients obtained poor results. Thus nonoperative treatment with the use of traction was a satisfactory procedure that could be used for all types of trochanteric fractures without selection. No further operation for removal of nail plate or screws was required and even extremely old patients were able to stand this treatment.

ITALY

Complement-Fixation Test for Brucellosis.—Gargani and Aleandri of the University of Florence (*Annali Sclavo,* June, 1959) prepared antigens by freezing and defrosting from strains of Brucella abortus and Brucella melitensis. With these antigens it was possible to differentiate by complement-fixation tests between infection by these two organisms in experimental animals. The complement-fixation test was more specific than the agglutination test and sometimes, mainly for human infection, more sensitive. The authors recommended that both reactions be used for a more exact diagnosis of brucellosis.

UNITED KINGDOM

New Medical School.—Work has begun on a new medical school at Bristol University. This new school is part of an expansion program to accommodate another 2,000 students in the next five years. It will be ready for occupation in 1962. It will contain three lecture theaters, one seating 250 students, which will also be used for medical congresses. A research block for investigations of radioactive isotopes and veterinary studies are part of the project.

Empty Beds at Plastic Surgery Hospital.—Beds are empty and equipment is idle in several wards at Queen Mary's Hospital, Roehampton, London, one of the important centers dealing with burns, skin-grafting, and plastic surgery. This is not due to lack of patients, many of whom are waiting for admission, but of nurses. Ever since the center was opened in April nearly half the beds have been empty because not enough nurses can be recruited. According to the chief nurse another 30 trained nurses are urgently required.

Drug-resistant Tuberculosis.—One of the major health problems of the future according to Prof. Frederick Heaf, of the Welsh National School of Medicine, will be drug and antibiotic-resistant tuberculosis. Deaths from pulmonary tuberculosis have declined rapidly to 4,000 a year, 20% of what they were a few years ago. This figure is low in comparison with the 29,000 deaths from bronchitis, 84,000 from coronary disease, and 20,000 from lung cancer, but this position may not be maintained if drug resistance increases. Professor Heaf advocates the immediate establishment of laboratories where drug resistance can be measured by a standard technique that can be used throughout the world. He suggests that a register of drug-resistant persons with tuberculosis be kept in every country. Attempts should be made to render them noninfectious, or if this cannot be done to reduce the virulence of the organism. Until new drugs or antibiotics are forthcoming such patients should be segregated from the rest of the population in industrial colonies, and their families should be supported. The highest mortality from tuberculosis in Britain is now in elderly men and young women. The Minister of Health is urging local health authorities to keep their registers of cases up to date.

Mannomustine.—It has been claimed by Hungarian workers that a complex of nitrogen mustard and mannitol, known as mannomustine or Degranol is more effective than nitrogen mustard itself in the treatment of leukemias and the reticuloses because it is more readily diffusible. Barlow and co-workers reported the results of a preliminary trial with the drug in 45 patients who had polycythemia, leukemias, and reticuloses (*Lancet* 2:208, 1959). They injected 100 mg. of the drug intravenously daily or on alternate days, the required dosage varying from patient to patient and with the particular disease. Twelve patients with chronic myeloid leukemia were given an initial course of 0.8 to 1 Gm. in single doses of 100 mg. while the leukocyte count was 80,000 to 150,000 per cubic millimeter and 1.2 to 1.8 Gm. when the initial count was over 200,000. Although moderate symptomatic improvement occurred in all patients between two and six weeks after the beginning of treatment, mannomustine was not considered to be as effective as the drugs at present in use, such as busulfan (Myleran), demecolcine, or nitrogen mustard hydrochloride. Temporary remission occurred in 83% of the patients with acute leukemia treated with mannomustine and prednisolone. Treatment appeared to be of value, particularly in the monocytic type, if the initial leukocyte count were much increased.

Mannomustine was found to be of some use in the treatment of chronic lymphatic leukemia, Hodgkin's disease, giant follicular lymphadenopathy, reticulosarcoma, multiple myeloma, and polycythemia. Complete regressions of lymphadenopathy and/or splenomegaly were obtained in 42% of the patients with Hodgkin's disease, and partial regression in the remainder. Although it had no effect on the final outcome, mannomustine appeared to relieve pain in 40% of the patients with advanced carcinoma with multiple secondary deposits. It produced severe marrow depression. Toxic effects from mannomustine were severe. Nearly 50% of the patients suffered from anorexia, nausea, or vomiting, particularly if more than 100 mg. was given. Some relief from these side-effects was obtained by adding 1 Gm. of ascorbic acid to the solvent used for the drug, and by the simultaneous administration of chlorpromazine. Anemia and leukopenia occurred in 33% of all patients and thrombocytopenia in 41%. There were painful local effects in some patients.

Supply of Drugs to Hospital Patients Excessive.—The Ministry of Health, in response to inquiries by the Central Middlesex Group Hospital Management Committee, has issued a statement urging hospital doctors to prescribe smaller quantities of drugs to patients when they leave the hospital to be treated by their own physicians. The matter arose because a patient who was discharged with more than 900 tablets of a potentially dangerous drug was found to be giving them away to children. Hospitals are now reviewing the supply of drugs in bulk to patients when they leave the hospital and when they are treated as outpatients. It is suggested that not more than seven days' supply of drugs be given to patients on discharge. It is the practice of some hospital doctors to issue a prescription valid for three months, with the patient calling at the hospital pharmacy every month for supplies. The hospital doctors argue that the patients may not visit their own doctors and that treatment might therefore be interrupted.

On the whole, general practitioners are more cost-conscious than hospital doctors because their prescriptions are checked by executive councils, and they can be questioned, or even fined, for what is considered to be excessive prescribing. The hospital doctor is free from this form of bureaucratic control. The Ministry of Health considered that while the discharge of a patient must rest with the hospital doctor, the return of the patient to the general practitioner should be considered as soon as possible if further treatment is needed after the patient leaves the hospital. Patients should not be treated as hospital outpatients if they could reasonably be referred to their general practitioner.

Shortage of Medical Teachers in Far East.—Because of the shortage of teachers of medical subjects in Indian, Pakistani, and Burmese universities and colleges, the Commonwealth Relations Office is appealing to British doctors to take short-term appointments in these countries. A two-year period is suggested. Sir George McRobert, who is medical adviser to the office, said that there are 20 vacant professorships in the countries mentioned. Readers and senior lecturers are urgently required on a temporary basis, and recently retired professors and teachers are being sought. Teachers are particularly needed in anatomy, physiology, pharmacology, pathology, bacteriology, and biochemistry. The salaries offered compare well with those obtainable in Britain, and a nontaxable allowance is given as an added attraction. The British council is advertising for occupants for seven vacant chairs in Baghdad University College of Medicine. In this university, as in some others in the Middle East, teaching is in English.

Prof. U. K. Sheth, of Bombay, speaking at the Second World Conference on Medical Education, said that there are 50 medical schools in India, and by 1965 the number is to be raised to 67. There is, however, an acute lack of teachers in these schools, particularly in the preclinical subjects. The staffs are either superannuated or young and immature. In clinical subjects the problem is complicated by the large amount of both inpatient and outpatient work, which leaves little time for teaching. Some help is being obtained from the Rockefeller Foundation.

Danger of Breast Abscess.—Hutchinson pointed out that in Britain breast abscesses may be responsible for the spread of infection in general hospitals (*Brit. M. J.* 2:277, 1959). Most of them occur in the puerperium, and if the confinement takes place in a maternity hospital or unit the responsible organism, Staphylococcus aureus, will most often be one of the antibiotic-resistant types. The abscess does not usually occur until some time after discharge from the hospital, and then the patient is usually sent to the surgical ward of another one, there to spread the resistant organism. Seventy-five strains of Staph. aureus were isolated from pus obtained at operation on 75 patients with a breast abscess who were sent to a general hospital. The antibiotic sensitivity to penicillin, streptomycin, chloramphenicol, the tetracyclines, and erythromycin was tested, and phage typing was done on 70 of the 75 strains. Patients were carefully questioned as to whether the abscess was puerperal, whether the confinement was in a hospital, and whether antibiotic treatment had been given previously.

Only 11 of the 75 strains were sensitive to all antibiotics. Forty-six came from patients with a known history, and 17% of them were sensitive to all antibiotics. Of the nonpuerperal strains 75% were sensitive to all antibiotics and 25% were resistant to penicillin alone. Of the puerperal strains only 5% were completely sensitive and 58% were resistant to penicillin alone. The difference between the number of strains sensitive to penicillin in the puerperal and nonpuerperal groups was highly significant, and suggested a fundamental difference in the origin of their staphylococci. Most of the polyantibiotic-resistant organisms belonged to phage types 80 and 52/52A/80. Hutchinson suggested that this reservoir of infection should be kept out of general hospitals, and that these patients should be nursed in infectious fever hospitals, which are half-empty at the moment. If it is decided to give an antibiotic, penicillin should not be chosen. It may be doubted if the use of any antibiotic is advisable since it fails to cure once the abscess has formed. When patients with breast abscesses are discharged from the hospital the general practitioner should be given the sensitivity data of the organism.

New Site for Royal College of Physicians.—The Royal College of Physicians of London has received a gift of $1,260,000 from the Isaac Wolfson Foundation for the building of new premises. The present college was built in 1925 in Pall Mall by Sir Robert Smirke to accommodate 90 fellows. Now there are 900 fellows and 4,000 members. A site has been acquired in Regent's Park and the generosity of the Wolfson Foundation together with the money from the sale of the existing building not only will provide for a new building but will enable the college to extend its activities. The Wolfson Foundation was established in 1955. The grant to the Royal College of Physicians is the largest the Wolfson Foundation has yet made.

Monitoring the Heart of the Fetus and Newborn Infant.—Continuous recording of the fetal heart sounds is desirable in such conditions as trial labor, prolonged labor, or difficult birth. MacRae has constructed a continuous monitoring device for the fetal heart (*Lancet* 2:266, 1959). A small microphone is strapped to the mother's abdomen over the area where the fetal heart is best heard and covered with plastic rubber to reduce extraneous sounds. The microphone is connected with a soniscope, which selects and amplifies the heart sounds, which are received through earphones and tuned to their optimum volume. The sounds can be picked up either by the latter or by a loudspeaker, which is adjusted to select the low-frequency sounds of the fetal heart. Toward the end of the second stage of labor the microphone has usually to be brought to the midline above the pubis because of rotation of the shoulders, and this allows recordings to be made until the head is crowned. Tape recordings can be made of the heart sounds or they may be recorded phonographically and a visual record obtained. Systole and diastole can then be accurately measured. The fetal heart sounds can be relayed outside the labor ward so that simultaneous check can be made on several patients.

MacRae used the monitoring device in cases of maternal complications during labor, when there was fetal distress, during the administration of oxytocin injection in labor, during forceps delivery, and whenever there was cause for anxiety. The instrument revealed reflex fetal kicks and tumultuous movements of distress, and during forceps delivery it could guide the strength and duration of traction. MacRae considered that continuous monitoring of the fetal heart is essential in the second stage of labor, when uterine contractions are more powerful and the fetal brain is subject to the stress of molding. Fetal distress may suddenly appear and timely warning of this is given by observing the heart sounds. In addition it is claimed that the cardiophone can play an important part in resuscitation of the newborn infant, when respiratory failure puts a strain on the heart, in following the progress of the baby born after a difficult labor, and in monitoring the heart of the newborn infant during exchange transfusion, which imposes an extra load on the heart, especially in premature infants or babies in shock.

Griseofulvin.—Cochrane and Tullett (*Brit. M. J.* 2:286, 1959) used griseofulvin in an agricultural area for the treatment of acute inflammatory cattle ringworm infections in man. The lesions were essentially nodular, boggy, exudative, circumscribed tumors studded with pustules. Frequently they were crusted and foul smelling, the neighboring lymph glands were enlarged and tender, and the patient suffered from mild malaise and fever. Several patients had acute active annular areas of ringworm. All had been in contact with cattle or farm buildings and culture from hairs or skin scrapings produced Trichophyton verrucosum. At first an initial daily dose of 2 Gm. of griseofulvin was given orally for one week and then reduced as the lesion responded to treatment. Later 1 Gm. daily was found to be adequate for resolution of the lesions, which took 12 to 21 days. Routine blood examinations and liver function tests revealed no abnormality.

Control cases in which patients were not given griseofulvin and were kept on routine standard treatment, which consisted of hot formentations, antiseptic lotions, and fungicidal ointments, took 9 or 10 weeks to clear. The most noticeable difference between the patients receiving standard treatment and those receiving griseofulvin, apart from the rapid resolution of the lesions, was the quick disappearance of general malaise, pain, and discomfort, and the early response of satellite lesions in those treated with the latter drug. In addition to these the authors successfully treated a number of patients with human ringworm due to T. rubrum, T. schoenleini, and Microsporon audouini.

Chronic Bronchitis.—Although chronic bronchitis is very prevalent in Great Britain, until recently few epidemiological investigations have been made on the disease. Fletcher and co-workers (*Brit. M. J.* 2:257, 1959) studied respiratory function and illness in 192 London postmen and 192 female employees in the London Post Office with a view to determining the incidence of the disease and its distribution in the sexes. The employees were given a questionnaire relating to symptoms, their sickness and absence records were inspected, and their ventilatory capacity and daily sputum volume were measured. A working criterion of bronchitis that was accepted was the expectoration of phlegm on most days during at least three months of the year. It was found that the men had more cough and produced more sputum than the women, but the prevalence of other symptoms and of chest illnesses was similar in the two sexes. There was an exacerbation of respiratory symptoms with age in the men, but not in the women. These differences were only partly attributable to differences in smoking habits. The degree of phlegm production was graded according to whether or not it occurred throughout the day, and this grading correlated well with the volume of sputum produced in the first hour after waking; 55% of the men habitually coughed up sputum, compared with 21.5% of the women. Ventilatory capacity was significantly impaired in the men with cough and sputum, but not in the women.

It is possible that the differences of expectoration in the sexes were due to the exposure of the men to the polluted air of London. They worked outdoors, while the women worked indoors. The striking lack of impairment of ventilatory function in association with cough and sputum and recurrent chest illnesses in the women suggested that bronchial hypersecretion and recurrent infection have rather different consequences in the two sexes. The authors suggested that chronic bronchitis should be diagnosed in subjects with a productive cough not due to other causes, and that it should be graded, according either to its severity or to the persistence of the symptoms throughout the day or according to the volume of sputum expectorated. They considered that disability from impairment of ventilatory capacity or recurrent illness should be regarded as complications, and not as essential features of bronchitis, as it is important to recognize the disease before it has resulted in disability.

Larger Babies.—A survey undertaken on behalf of the Ministry of Health at the request of the British Pediatric Association and covering nearly 20,000 children in 11 urban and rural areas of England and Wales showed that the average weight at birth is increasing. The average weight has increased from 7 to 7.53 lb (3,175 to 3,345 Gm.) for boys and 7.2 lb. (3,245 Gm.) for girls (Ministry of Health Reports on Public Health and Medical Subjects No. 99, Her Majesty's Stationery Office). The standards of normal weight in infancy accepted hitherto were based on data collected many years ago. The Ministry report suggests that in infant welfare clinics, hospitals, and general practice the revised standards should be used. The largest proportion of underweight births occurred among the children of unskilled workers. The largest proportion of high-weight births was in babies born of parents in the professional and managerial classes.

The birth weight was found to rise from the first-born to those born later. In the survey four phases of growth could be distinguished in children from birth up to the age of 3 years. For the first four weeks growth was variable. A rapid increase occurred up to the age of 4 months, when the average boy's weight was 14.5 lb. (6,520 Gm.) and the average girl's was 13.75 lb. (6,152 Gm.). Then the rate slackened off. At one year of age the average weights for boys and girls were 23 and 21.5 lb. (10.4 and 9.5 kg.) respectively. Then growth took place at a fairly uniform rate until at 3 years of age the average boy weighed 32.5 lb. (14.7 kg.) and the average girl 31.5 lb. (14.3 kg.). This gain in weight, except in the first few months, was largely independent of the birth weight. It was in the first few months of life that the child who was underweight at birth grew more rapidly than the child of normal birth weight.

Perceptual Isolation.—Much evidence suggests that continual sensory bombardment is necessary for the maintenance of consciousness, awareness of the subject's relationship to his environment, and intelligent adaptive behavior. Smith and Lewty tested normal volunteers isolated as far as possible from all perceptual stimuli (*Lancet* 2:342, 1959). To eliminate all sensory input was manifestly impossible, but ingenious devices were used to reduce it to a minimum. The subjects were kept in cubicles suspended on nylon cords in isolated soundproof rooms, which were approached by a series of soundproof doors. A special ventilation plant was installed, all sound from fan motors being excluded by means of special silencers. Plugs and wiring for tape-recorders and microphones were provided between the observation room and the suspended cubicle and provision made for encephalographic recording. The subjects were allowed to rest on a bed or walk about to avoid muscle cramps. Their eyes were covered with translucent goggles to eliminate patterned vision, and their hands and arms were enclosed in cotton gloves and padded gauntlets to reduce tactile sensation. Meals were eaten in isolation. The volunteers were visited four times a day, but not at regular times, to test their appreciation of time.

Twenty volunteers (11 women and 9 men) were tested. The longest period spent in complete isolation by any one of them was 92 hours 20 minutes and the shortest was just under 6 hours. The women held out better than the men, the average isolation times of the two being 29 and 49 hours respectively. Apart from many individual reactions, a general sequence of events was observed: increasing sleep, followed by restlessness and agitation, followed by thinking difficulties, and finally panic. Thinking became disordered in all those who survived the test for any length of time. In many, concentration was completely lost and in 12 of the subjects disordered thinking produced fear and panic. Attacks of unbearable anxiety, tension, or panic were the main reasons for abandoning the test, which all subjects could do voluntarily by pressing a button.

All became agitated and restless, both subjectively and objectively. Appreciation of time was lost, most of the subjects overestimating it. Body image disturbances, particularly of the head and arms, occurred in seven of the subjects, and dreams, which were frequent, reached a nightmare intensity in five when tension and anxiety were mounting. Irritability was observed in only two subjects. The amount of time spent in sleep was correlated with the ability to spend a long period in isolation. The appetite was good at first, but progressively deteriorated in those who spent a long time in isolation.

A psychiatric questionnaire given to all the subjects revealed that the placid and calm person with an intelligence level of, or somewhat below, average is more likely to submit to prolonged sensory deprivation. Two subjects who abandoned the test after five hours were anxiety-prone and worrying personalities. Smith and Lewty believe that sensory deprivation is an important psychiatric tool.

BCG and Vole Bacillus Vaccines.—A controlled clinical trial of BCG and vole bacillus vaccines in the prevention of tuberculosis was started in 1950 under the direction of the Medical Research Council, which published its first report in 1956. The second report appeared in the *British Medical Journal* (2:379, 1959). There were 56,700 participants originally in the trial, all of them children aged 14 to 15½ years and about to leave school. They are now aged between 21 and 24 years. The children were initially tuberculin-tested and had a roentgenogram of the chest. Those found to have active tuberculosis were excluded from the trial. Those with normal chest films, but a positive tuberculin-test, were followed up in the same way as those in the vaccinated and control groups. The tuberculin-negative children were randomly divided into vaccinated and unvaccinated control groups. About 90% of those taking part in the trial were subsequently contacted personally by Medical Research Council teams, through the mail, or through National Health Service or armed forces physicians. All patients with definite and suspected cases of tuberculosis were examined by independent doctors for final diagnosis; to avoid bias the doctors were unaware of the history of each subject.

This second report gives the results for all participants who have been in the trial for five years, with preliminary but incomplete data up to seven-and-a-half years. The annual incidence of tuberculosis in the BCG-vaccinated group was 0.38 per 1,000 compared with 2.29 per 1,000 among those in the tuberculin-negative unvaccinated group who were admitted to the trial concurrently. This represents a reduction, attributable to vaccination, of 83%. Over the same period the annual incidence of tuberculosis in the vole bacillus–vaccinated group was 0.33 per 1,000 compared with 2.62 per 1,000 among the tuberculin-negative unvaccinated group —a protection rate of 87%. The vole bacillus was not associated with the development of lupus vulgaris at the site of vaccination, a complication which had been reported previously. The degree of protection with both BCG and vole bacillus vaccines was similar for tuberculous pleural effusion, pulmonary tuberculosis, and hilar gland enlargement. Four cases of tuberculous meningitis and four of miliary tuberculosis were found among the negative unvaccinated participants, but none among the vaccinated. There was a suggestion that the lesions in the vaccinated subjects were less extensive, judged radiologically, and less severe, judged clinically, than those in the negative unvaccinated subjects.

The trial has thus shown that BCG vaccine given to children 14 to 15½ years of age confers appreciable protection against tuberculosis, lasting for at least five years and possibly longer. As tuberculosis occurred to a large extent in children with a positive tuberculin test but no radiologic evidence of infection at the beginning of the trial, it is suggested that perhaps the vaccine might be given at an earlier age, when fewer children are infected. Since the beginning of the trial the proportion of tuberculin-positive children has fallen rapidly in most areas in Britain. So far relatively few children in the country have been immunized with BCG vaccine.

Sickle-Cell Disease.—Sickle-cell disease is characterized by an abnormal hemoglobin molecule, which in its reduced form aggregates to form a gel and distorts the shape of the red blood cell. This condition, which is a cause of anemia and bizarre symptoms, particularly in pregnancy and conditions of stress, has hitherto been reported only in the United States and Africa. Five cases seen in a London hospital in West Indian and African immigrants were described by Diamond (*Lancet* 2:322, 1959). All the patients were Negroid, and in all there was mild to severe anemia, sickling of the erythrocytes at reduced oxygen tension, numerous target cells in the peripheral blood film and decreased osmotic fragility of the red blood cells. Four of the patients were women and in all of them the condition presented as an anemia associated with pregnancy or the puerperium. The disorder often remains undiagnosed because the hemolysis that occurs is compensated by increased activity of the marrow. An additional demand on reserves (in these four patients it was pregnancy) drew attention to the anemia. The fifth patient was a man whose presenting complaint was sciatica. Electrophoresis of the hemoglobin confirmed that all five patients' symptoms were examples of sickle-cell hemoglobin-C disease.

CORRESPONDENCE

VASCULAR ACCIDENTS ASSOCIATED WITH NECK MANIPULATION

To the Editor:—The article entitled "Vascular Accidents of the Brain Stem Associated with Neck Manipulation" by Green and Joynt, in THE JOURNAL, May 30, 1959, page 522, brought back to my mind a comparable series of three patients, all in the same family, who were "treated" by the same chiropractor. Oddly enough, one patient, a 24-year-old woman, certainly had an onset of multiple sclerosis, and the chiropractor was consulted because of numbness of an upper extremity. After the initial manipulation by the chiropractor there was a complete paralysis of the entire extremity, dizziness, vomiting, slurred speech, and visual disturbances. Three weeks prior to this, the mother of the patient was manipulated by the same chiropractor, who "adjusted the neck vertebrae," with a resulting paralysis of both upper extremities and a similar group of symptoms. Two months after the daughter recovered the father of the patient was manipulated by the chiropractor and also developed similar symptoms. In all three patients there were positive x-ray findings and spinal fluid disorders. The parents made complete recoveries, but the daughter has had several exacerbations and remissions of her multiple sclerosis in the past 12 years and still has a paretic left arm.

LOUIS D. BOSHES, M.D.
55 E. Washington St.
Chicago 2.

EXCHANGE TRANSFUSION FOR ASPIRIN POISONING

To the Editor:—Dr. Sterne's article "Exchange Transfusion for Aspirin Poisoning" in THE JOURNAL, Aug. 15, page 1924, requires comment. We agree with the author that aspirin poisoning is a real danger in infancy and that exchange transfusion has a place in therapy, but we cannot agree with the management of the presented case. It is stated that the child received 0.75 Gm. of aspirin in the preceding 48-hour period. Assuming that the child weighed 10 lb. (4,536 Gm.), which seems reasonable in light of the 100-cc. blood transfusion and stated age of 6 weeks, this does not represent a toxic dose when given over a two-day period. Nelson's "Textbook of Pediatrics" states that a dose of about 150 mg. per kilogram given over a short period of time represents a toxic dose. Further proof that the level in all probability was not toxic is the statement that the blood salicylate level was 23 mg. per 100 ml. in this dehydrated patient. Toxicologists give 30 mg. per 100 ml. as a toxic level. It is stated that the blood carbon dioxide level was normal, and a urinary or blood pH is not mentioned.

It is significant that after intravenous fluid therapy the pH had risen to 7.9, a level that most textbooks state is incompatible with life. At this time two exchange transfusions were performed and the child was reported as improved. The exchange transfusions helped to treat the child's congestive failure by removing 110 cc. of blood and lowering the elevated venous pressure and no doubt correcting the iatrogenic acid-base imbalance. Since the blood salicylate level was precisely the same after two exchange transfusions, despite the marked clinical improvement in the patient, it seems unlikely that the original symptom complex was due to salicylism. We believe that when exchange transfusion is used to correct iatrogenic disease, it is the responsibility of the author and the journal to report it as such.

FRANK A. OSKI, M.D.
SHERWOOD SALITSKY, M.D.
Hospital of the University of Pennsylvania
Philadelphia 4.

The above comment was referred to the author of the article cited, and he has submitted the following reply.

To the Editor:—In cases of poisoning in infants, it is generally conceded that the exact amount of the toxic substance ingested is open to question. The mother was somewhat vague as to the exact amount of aspirin given this infant. As stated in the article, the salicylate level before the first exchange was 35 mg.%, fell to 29 mg.% thereafter, and to 23 mg.% only after the second transfusion. Intravenous fluid therapy consisted of 5% dextrose solution in distilled water and a whole blood transfusion. No alkali was given so that this perhaps was not an iatrogenic acid-base imbalance, as suggested by Drs. Oski and Salitsky. The whole blood transfusion was given in an attempt to buffer the acid-base relationship and also because of a mild anemia (a hemoglobin level of 10 Gm.% despite the dehydration), the cause of which was not ascertained.

It was my impression that the exchange transfusions had aided in correcting the acid-base imbalance as well as in reducing the salicylate level from 35 to 23 mg.%. The dramatic improvement after the exchange transfusions led me to believe that such therapy was beneficial. Whether this was due to the correction of the acid-base imbalance or to a reduction of the salicylate level or both is unknown. The elevated venous pressure might have been due to the vigorous fluid therapy, despite the fact that the amount given was calculated using the generally accepted criteria. It might also have been due to the infants' marked activity at the time it was measured. Despite the fact that a deficit of 110 cc. of blood was established, the venous pressure remained at 30 cm. This deficit was decreased to 85 cc. at the second transfusion, and yet the venous pressure fell to 11 cm. The fall in venous pressure could be clinically correlated with the patient's activity.

I appreciate the interest of Drs. Oski and Salitsky but would suggest that they reread the article. I would be happy to give a detailed account of the case if they so desire and would welcome any further criticism.

Thomas L. Sterne, M.D.
2701 N. Azalea St.
Victoria, Texas.

BISHYDROXYCOUMARIN TOXICITY

To the Editor:—The article by Eisenberg on bishydroxycoumarin toxicity in The Journal, Aug. 29, page 2181, requires comment. The following points are open to discussion:

There was no justification for dividing the daily dose of this anticoagulant. It has been generally recommended that the total daily dose should be taken only once in order to avoid confusion. There is no guarantee that this medicament could not have been taken five or six times during the day. Some physicians give long-acting substances only once every few days.

A dose of 200 mg. of bishydroxycoumarin is generally a large one. Most patients can be maintained on less than 100 mg. daily. When a patient needs more than 100 mg. daily, and particularly if he exceeds a weekly dose of 1,000 mg., he exhibits at least a partial resistance to the drug and another anticoagulant should be used. In such a case, very small doses of other substances will usually decrease the prothrombin time well. If, however, one continues to use an excessive dosage of bishydroxycoumarin, one takes the same risk as with large doses of insulin in resistant patients. There might be a sudden change of sensitivity to the drug.

This patient returned with epistaxis. His prothrombin time (21% of normal) would hardly be low enough to cause such bleeding. There must have been some local lesion in the nose. If, however, the laboratory test was wrong, there is practically always hematuria and cutaneous bleeding preceding epistaxis. Those symptoms were not mentioned at all, but it was noted that there was no gross or occult bleeding in the stool, a circumstance that never occurs unless one is dealing with a grossly neglected patient who has bleeding from many sources or with a patient who has coincidental gastrointestinal ulceration.

This patient was readmitted to the hospital on account of headache, but again no statement was made in regard to cutaneous and urinary bleeding. It would be most unusual to have a subdural bleeding alone, not accompanied by other signs of hemorrhagic diathesis.

A brain operation was performed without previous determination of the prothrombin time and without correction of this abnormally lowered value to normal. This is a prerequisite for all brain operations.

No clear-cut evidence was given that the inability to regain consciousness by the patient was a sequela of the bishydroxycoumarin treatment. It could just as well have been caused by the brain operation.

Heinz B. Eisenstadt, M.D.
2301 Procter St.
Port Arthur, Texas.

The above comment was referred to the author of the article cited, and he has submitted the following reply.

To the Editor:—Dr. Eisenstadt is correct in pointing out that bishydroxycoumarin is not generally given in divided dosages and that 200 mg. per day is an uncommonly large amount. My original protocol read "50 mg. q. d."; it was misinterpreted by the editors as "50 mg. q. i. d.," or four times the intended amount, and the error was overlooked in proofreading.

Dr. Eisenstadt is misinformed in believing that a prothrombin time of 21% "would hardly be low enough to cause the nose bleeding." A number of authors have pointed out that no reliable relation can be discerned between the onset of hemorrhage and the prothrombin, bleeding, or coagulation times. While it appears desirable to maintain a prothrombin time of 15 to 25% of normal in a patient taking bishydroxycoumarin, intravascular clotting has occurred at lower and hemorrhagic diathesis at higher levels.

As pointed out in the protocol, "blood studies performed preoperatively but reported postoperatively revealed a prothrombin time of 8%." While I believe that most physicians would agree that, ideally, prothrombin time should be in the normal range before elective brain surgery, the rapid deterioration of this patient required immediate removal to the operating room. Emergency subdural decompression was in order irrespective of the patient's laboratory determinations, which, as a matter of fact, were made available as the procedure was nearing completion.

The patient's coma and subsequent death were both attributable to the effects of the subdural hematoma. Physicians experienced in the care of these patients are familiar with the observation that once coma has occurred consciousness is not always regained, even in the event of successful decompression. Postmortem study of the brain, as described in the protocol, revealed about 5 cc. of clotted blood and moderate cerebral edema. No other abnormal findings were noted.

M. Michael Eisenberg, M.D.
313 Carlyle Pl.
Alexandria, Va.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Iproniazid in Angina Pectoris: A Double-Blind Study. M. Shoshkes, E. L. Rothfeld, M. C. Becker and others. Circulation 20:17-24 (July) 1959 [New York].

A "double-blind" experiment was performed with 4 unknowns, 2 of which were iproniazid and 2 were placebos, given separately at monthly intervals to 23 patients, aged between 52 and 85 years, with ischemic heart disease associated with angina pectoris. Hypertension was present in about half of the patients. The initial dose of one 25-mg. tablet administered twice daily was reduced satisfactorily to 25 mg. a day for those who remained cooperative until the end of the investigation. The use of iproniazid was judged effective in relieving the pain of 14 patients (64%) and of 16 patients (73%) of the series on 2 separate periods, whereas the placebos were effective in only 6 patients (30%) on 2 separate periods. The first use of iproniazid produced an increase in incidence of untoward reactions in 6 patients (27%) and by the second month in 11 patients (50%). Most of the reactions were mild in nature.

The effects of iproniazid were thus slowly cumulative, as shown by an increasing rate with time of both therapeutic effectiveness and untoward side-effects. It is likely that, except for a possible specific hepatotoxicity, other reported side-effects were manifestations of overdosage. The drug also produced a mild hypotensive effect, as well as an elevation of mood, and aided in maintaining body weight. There was no change in the clinical course or in the progression of the primary heart disease. The authors recommend a daily dose level of iproniazid of no more than 50 mg. Doses of over 50 mg. a day should be used only initially and not in ambulatory patients. When a therapeutic effect is achieved, the maintenance dose of the drug should be continually reduced in step-like fashion at 1-or-2-week intervals until the minimum effective dose is found for the individual patient.

Triamcinolone Therapy in Chronic Bronchial Asthma. L. Levin and E. Schwartz. New York J. Med. 59:2710-2715 (July 15) 1959 [New York].

Triamcinolone (Aristocort) was administered to 50 patients as a supplement to symptomatic, local, and immunological management of intractable bronchial asthma. These 50 patients included persons of both sexes, and their ages ranged from 3 to 75 years. The administration of any other steroid was suspended before starting the triamcinolone treatment. Most patients received an initial dose of 6 to 8 mg. (in 74% of the cases) and a maintenance dose of 1 to 4 mg. (in 62% of the cases). The duration of the treatment was from 1 to 8 months for 39 patients and from 1 to 9 months for 11 patients suffering from severe asthma.

The results of triamcinolone therapy were excellent in 26 cases (52%), good in 20 (40%), and fair in 4. Excellent results meant that the patients became entirely free of asthma symptoms and remained so; good results meant that the patients were fairly free of symptoms, with only an occasional recurrence; fair results meant that the patients experienced relief in the severity of their symptoms and felt satisfied even if there remained some wheezing. Twenty patients in the excellent-result group, 13 in the good-result group, and all 4 in the fair-result group required a daily maintenance dose of only 1 to 4 mg.; the others required a dose of 1 to 16 mg. Besides the relief in their symptoms, the patients experienced a degree of satisfaction and encouragement that helped obtain their cooperation in continuing with the treatment. Side-effects occurred in 8 patients, but they were not severe enough to necessitate discontinuance of the therapy or a decrease in the dosage. Triamcinolone was found to be a useful drug in the management of chronic intractable asthma, especially because of the comparatively small doses required and the infrequency of side-effects.

Experiences with Tolbutamide in a Diabetic Clinic. J. Levine, N. T. Gottlieb and M. Tischler. New York J. Med. 59:2567-2569 (July 1) 1959 [New York].

Studies were carried out with the oral administration of tolbutamide for from 8 to 12 months to 77 patients with diabetes, at the diabetic clinic of Coney Island Municipal Hospital. Only those patients were selected for this study who used 40 units or less of insulin daily, who had no history of repeated ketosis or acidosis and no significant renal or hepatic dysfunction, and who responded to a

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The place of publication of the periodical appears in brackets preceding each abstract.

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loading dose (tolerance test) of 3 Gm. of tolbutamide by a 25% or greater fall in the fasting blood sugar 4 hours after administration of the dose. These patients were given 3 Gm. of tolbutamide (6 0.5-Gm. tablets) in divided doses for 3 days; 2 Gm. (4 tablets) in divided doses for the next 3 days; and 1 Gm. (2 tablets) on the 7th day. Insulin dosage was gradually reduced over a period of 4 days as tolbutamide therapy was instituted in some patients requiring more than 25 units of insulin, so that by the 5th day insulin was withdrawn. The maintenance dose was then adjusted at from 1 to 4 tablets of tolbutamide daily, depending on the follow-up studies on urine and fasting blood sugar, and on the well-being of the patient. No change was made in the regimen other than the substitution of tolbutamide for insulin.

The observations showed that in several patients who responded well to the test dose the diabetic control was not maintained by tolbutamide. Eight such patients were returned to insulin therapy, and were considered failures. In the remaining 69 patients the diabetes was well controlled or improved. There was no evidence of toxicity in any patient. The authors believe that the improvement obtained in diabetic control in this series should not be attributed to the effect of tolbutamide alone, but also to the fact that this hypoglycemic agent can be taken easily, and that, therefore, the patients used it regularly.

The Toxico-Cancerous Syndrome: Its Value in Early Diagnosis and Immediate Prognosis. M. L. Gratacós. Semana méd. 66:873-876 (June 25) 1959 (In Spanish) [Buenos Aires].

The author presents his concept of the toxicocancerous syndrome developed from observation of cancerous patients at various stages. This syndrome is characterized by comparative tachycardia, i. e., tachycardia without any elevation of temperature or any alteration in respiratory rhythm and blood pressure. A table containing the average pulse and temperature values in 42 patients with cancer of different types and localizations shows this negative correlation between tachycardia and temperature. The pulse frequency varies from 64 to 130, while the temperature varies from 35 to 38 C (95 to 100.4 F), without any correlation in any individual case. These average figures were obtained by taking the temperature and counting the pulse approximately 52 times for each patient (in the morning, at noon, and at night). It is the author's conclusion that the combination of tachycardia, normal temperature or hypothermia, normal blood pressure, and normal respiratory rhythm has a diagnostic and prognostic meaning in cancer. As a diagnostic criterion this syndrome should alert the physician to the possibility of a cancerous condition and call for immediate confirmation by glycoprotein determination. As a prognostic criterion, the greater the difference between pulse and temperature, the more serious is the patient's condition. The lowest condition is indicated when the pulse exceeds 110, while the temperature falls below 36 C (96.8 F). As a palliative treatment of the syndrome, the administration of antitoxins, liver extracts, carboxylase, and vitamins, as well as blood transfusions, are recommended.

The Influence of Chemotherapy on Survival in Acute Leukemia: Comparison of Cases Treated During 1954 to 1957 with Those Treated During 1947 to 1954. A. Haut, S. J. Altman, M. M. Wintrobe and G. E. Cartwright. Blood 14:828-847 (July) 1959 [New York].

The authors report the longevity, reckoned from the symptomatic onset of acute leukemia, as well as from the initiation of treatment, and observed in a group of 89 patients who were treated at the University Hospital in Salt Lake City, between 1954 and 1957. They have compared their findings in this group of patients with those in a similar group of 78 patients treated at the same hospital between 1947 and 1953, i. e., before the availability of chemotherapeutic agents. The median survival of all patients, considered as a unit, was increased from 3 to 6 months, as measured from the date treatment was begun. The change was found to be as statistically significant as it was clinically important. The longer survival observed in the group of patients treated between 1954 and 1957 correlated with the more general administration of 3, rather than 2, chemotherapeutic agents, such as mercaptopurine, steroids, and folic acid antagonists. The significant factor, therefore, appeared to be the number of effective agents administered, rather than the use of any one in particular.

On analysis, improved survival was statistically proved only for patients with lymphoblastic leukemia; for these the median survival was 10 months after the symptomatic onset of leukemia and 7½ months after the institution of treatment. Within this group, there was an even greater improvement for those whose leukocyte values immediately before the institution of therapy were less than 10,000 per cubic millimeter; 50% of these patients lived more than 12 months after treatment was begun. The reason for the exceptional longevity of patients with the lower pretreatment leukocyte values is unknown. It appears that one can attribute at least part of the improvement to therapy. The type of statistical analysis used presents the minimum figures for improvement in median survival. When the ultimate longevity is known for the 17% of the patients surviving at the closing date of the study, an additional small increase may be found. The relative inefficacy of chemotherapy in myeloblastic leukemia should be a signal for greater screening of new agents in this type of tumor.

The Association of Peptic Ulcer with Hereditary Hyperparathyroidism. C. E. Jackson. Gastroenterology 37:35-37 (July) 1959 [Baltimore].

The author reports on a family in which hyperparathyroidism was present in at least 2 members, a 31-year-old man and his 55-year-old father. These 2 patients and, in addition, a paternal uncle and his daughter had peptic ulcers. Although further investigation of this family did not reveal any additional definite cases of hyperparathyroidism, the occurrence of several cases of peptic ulcer in a family in which hyperparathyroidism was present in at least 2 members has suggested that the high incidence of peptic ulcer associated with hyperparathyroidism may be related to some factor in the hyperparathyroid person which brings out the underlying ulcer tendency. The high incidence of the association of these 2 diseases may be a reflection of the frequency of peptic ulcer tendency in the general population.

Serum Lactic Dehydrogenase and Serum Transaminase in Human Leukemia. G. B. Magill, F. Wroblewski and J. S. La Due. Blood 14:870-881 (July) 1959 [New York].

The authors performed estimations of serum lactic dehydrogenase (SLD) and serum glutamic oxalacetic transaminase (SGO-T) concentrations in 56 adult patients and 10 children with leukemia. Elevated SLD levels were observed in 23 (77%) of 30 adults with acute leukemia, in 7 (70%) of 10 children with acute leukemia, in 15 (94%) of 16 adult patients with chronic myelocytic leukemia, and in 6 (60%) of 10 adult patients with chronic lymphocytic leukemia. The degree of the elevation of the SLD level appeared to be significantly greater in the chronic myelocytic than in the chronic lymphocytic group. Serial determinations of the SLD level were performed for periods of from 1 to 82 weeks in 55 patients of whom 43 had elevated levels at one time or another. Of these 43 patients, 21 were adults with acute leukemia, 5 were children with acute leukemia, 12 were adults with chronic myelocytic leukemia, and 5 were adults with chronic lymphocytic leukemia. Fair to good correlation between the SLD level and conventional parameters of leukemic activity was noted in 7 (33%) of the 21 adults and in 2 (40%) of the 5 children with acute leukemia, in 8 (67%) of the 12 adults with chronic myelocytic leukemia, and in 1 (20%) of the 5 adults with chronic lymphocytic leukemia. At the present time the mechanism by which the SLD concentration is elevated in patients with leukemia is not clear. The most attractive concept as to the source of elevated SLD concentration in leukemia is that of more rapid leakage of enzyme from more fragile cells. The lack of over-all correlation between serial SLD levels and established parameters of leukemic activity has proved to be disappointing in regard to the clinical usefulness of determinations of SLD levels in leukemia.

Serum glutamic oxalacetic transaminase (SGO-T) levels were studied in 61 patients. Levels greater than 100 units were seen in only 8 patients, of whom 7 had either viral or toxic hepatitis and 1 had terminal septicemia. Other types of liver impairment, including leukemic infiltration, were associated with normal or slightly elevated SGO-T levels. If these differences could be confirmed by additional studies, a SGO-T level of more than 100 units in a patient with leukemia associated with jaundice would suggest either a viral or a toxic type of hepatitis. The presence of a normal or slightly elevated SGO-T level in a patient with leukemia associated with jaundice or other evidence of hepatic involvement would be compatible with leukemic involvement of the liver.

The Association of Nonspecific Jejunitis and Granulomatous Phlebitis in the Legs. J. A. H. Collyns. Gastroenterology 37:64-72 (July) 1959 [Baltimore].

The author reports on a 26-year-old man with jejunitis, apparently isolated as regards the gastrointestinal tract but complicated by an unusual peripheral superficial phlebitis not itself producing symptoms. There was a history of several bouts of colicky abdominal pains in the umbilical region, each of 5 to 6 days' duration. At no time had there been any diarrhea or constipation. Administration of sulfaguanidine tablets seemed to bring relief, but periodic moderately severe pains in the umbilical region persisted during the ensuing 15 months. The patient was readmitted to hospital for an attack of severe central abdominal pain with temperature up to 101 F (38.3 C), and barium meal examination revealed stasis and dilation in the proximal part of the jejunum. A nodular length of nonpulsating vessel was discovered in the position of the left long saphenous vein, midway between knee and ankle. At biopsy the vessel was regarded as a vein that had been occluded by old thrombosis.

An exploratory laparotomy was performed, which revealed severe inflammation of a segment of the upper jejunum. The serosa was covered with small white "miliary" nodules. A diagnosis of isolated segmental jejunitis, either tuberculous or of the nonspecific "Crohn" variety, was made, and it was decided to try the effect of antituberculous drugs. After removal of an apparently normal appendix the abdomen was closed. A nodular, 2-cm.-long segment of vessel complete with overlying skin was removed from midway between the right knee and ankle. Histologically the picture was that of a granulomatous panphlebitis in a vein of moderate size. Despite active antituberculous therapy with streptomycin, aminosalicylic acid, and isoniazid, the condition of the patient did not improve, and laparotomy was repeated 3 months after the first intervention. Thirty-nine inches of jejunum were resected, which both macroscopically and microscopically showed the classic pathological picture of regional enteritis. Postoperatively the patient almost at once became free of abdominal pain. He made a complete recovery. Although frequent thorough searches have been made, superficial vascular lesions have never subsequently been discovered.

It is felt that the vascular lesions in this patient may have constituted an unusual superficial "Crohnide" reaction, dependent on and secondary to the deep-seated intestinal inflammation. The administration of sulfaguanidine at various times during the 15 months preceding the first surgical intervention might not have been entirely innocuous in this patient. The superficial phlebitis is grouped on morphologic grounds with temporal arteritis, and clinically with the other extra-alimentary manifestations of regional enteritis. The combination of lesions is unique.

Bacteriologic Culture of the Diseased Human Liver. J. M. Stormont, J. E. Mackie, E. H. Kass and C. S. Davidson. Ann. Int. Med. 51:17-22 (July) 1959 [Lancaster, Pa.].

The authors made bacterial cultures on liver tissue from 20 patients on the wards of the Boston City Hospital. Thirteen had cirrhosis of the alcoholic, 2 had hepatolenticular degeneration, and 1 patient each had cirrhosis of the alcoholic and acute homologous serum hepatitis, cirrhosis of undetermined type and acute cholangitis, cirrhosis of undetermined type, fatty liver, and congestive hepatomegaly. In the 12 patients with temperatures over 100 F, the fever was presumably caused by chronic pulmonary inflammation in 2, pulmonary tuberculosis in 2, and staphylococcic pneumonia, tuberculous peritonitis, acute cholangitis, miliary tuberculosis, and acute pancreatitis in 1 each. In 2 patients acute hepatic decompensation with cirrhosis and necrosis was the only evident explanation; in one of these patients this impression was confirmed at autopsy. One patient had subacute yellow atrophy which was felt to be secondary to homologous serum hepatitis. Cultures were obtained either from a Vim-Silverman needle biopsy specimen (14 patients) or by aspiration (6 patients) with use of a no. 20 spinal puncture needle. Aspiration culture was used when liver biopsy was contraindicated, i. e., when there was low blood prothrombin activity or poor patient cooperation. In the latter instances, standard biopsy technique was used, with iodine and alcohol preparation of the skin. When the stylus was removed, a 20-ml. syringe was attached, the needle was advanced into the liver, and suction was applied for about 4 seconds. A few drops of fluid were obtained and introduced into 3 to 5 ml. of the culture medium by rinsing the syringe once with sterile broth.

The culture mediums used were beef heart infusion broth with 5% horse blood, and chopped meat mediums for anaerobic cultures. The inoculated mediums were plated in nutrient agar and counted, were diluted for bacterial count, and were also incubated for from 1 to 4 days. If the incubated mediums showed evidence of growth, they were then subcultured. A loopful of each culture was also streaked on blood agar and eosin-methylene blue agar. Previous use of quantitative technique in the analysis of urinary tract infections had indicated that separation between contamination and infection may often be achieved on the basis of bacterial numbers in the urine. It is hoped that this method may also distinguish contamination from infection for liver cultures.

Bacteria were recovered from the liver in only one instance, and a colony count of over 100,000 per milliliter suggested that it did not represent contamination. The organisms were identified as Escherichia coli. The patient was a chronic alcoholic, with anorexia, weight loss, mild jaundice, and an intermittent spiking fever. A Vim-Silverman biopsy and culture were performed, and a diagnosis of mild cirrhosis with portal inflammation was suggested. Laparotomy later confirmed the presence of acute and chronic cholecystitis with common duct stones and cholangitis.

The authors feel that the data that are presently available suggest that bacteria are not ordinarily found in the human liver or portal vein blood, but that bacteria may invade the portal vein under unusual physiological circumstances, such as abdominal trauma, surgery, irradiation, shock, anoxia, or other circumstances leading to local changes in the intestinal wall. Why biliary stasis is particularly related to the retention of bacteria in the liver is not yet clear.

Cushing's Syndrome: Clinical Differential Diagnosis and Complications. L. M. Hursthal and J. B. O'Sullivan. Ann. Int. Med. 51:1-16 (July) 1959 [Lancaster, Pa.].

The authors reviewed the records of 34 patients with Cushing's syndrome seen at the Lahey Clinic, Boston, in the hope that a better understanding of the onset of the disease and its earlier recognition would result. At the time the 34 patients (7 males and 27 females) came to the clinic, the disease was in a more advanced stage than that which the authors attempt to delineate. In general, their symptoms and signs were about the same as those published on similar groups of patients. Surgical confirmation was obtained in 27 patients (adrenal carcinoma was found in 1, adrenocortical adenoma in 5, adrenocortical hyperplasia in 19, and aberrant adrenal tissue in the pancreas in 2). The remaining 7 cases were diagnosed by the characteristic clinical signs and laboratory findings when first seen on an average of 5 years after the onset of the disease.

Inquiries about the details of onset revealed that it was rapid in 24 of the patients. Such a high incidence (71%) of rapid onset was contrary to expectation; furthermore, the rapidity of onset did not indicate the underlying etiology. A case was placed in the group with rapid onset, if the initial symptoms were rapid enough to alert both the patient and the physician. The etiological diagnosis in these 24 patients was: adrenocortical hyperplasia in 19 cases; adrenocortical tumor in 3; carcinoma in 1; adrenal tissue aberrant in the pancreas in 1. The disease began with edema of the legs and face, described as "swelling," "bloating," and "puffiness," accompanied by some other signs, such as amenorrhea, renal colic, acne, hirsutism, bruises, weakness, mental symptoms, or diabetes mellitus. Other patients complained of a sudden craving for food with increase in weight, one patient having an increase of 40 lb. in one month. In 2 cases the initial symptom was renal colic with facial edema; the edema commenced one week before the renal colic in one patient, and 2 weeks after in the other. One of these patients had had 3 attacks of renal colic at yearly intervals. It was interesting that the onset in one patient was associated with symptomatic diabetes mellitus, and that a perforated duodenal ulcer occurred in a patient with episodic onset of symptoms.

There were 10 cases with gradual onset, including 2 cases resulting from an adrenocortical adenoma, and 1 with adrenal tissue aberrant in the pancreas. The clinical manifestations began with mental changes, oligomenorrhea, gradual weight increase, hypertension, sterility, and diabetes mellitus. In commenting on possible precipitating factors, the authors say that some patients described emotional strain before the onset of symptoms. In 6 patients, initial symptoms occurred after periods of unusual stress: a change of employment in one case, after marital separation in another, during a time when 3 jobs were held simultaneously in a third, when in solitary confinement after a prison riot in a fourth, working extra-long business hours in a fifth, and during a honeymoon in the sixth patient. Another precipitating or aggravating factor was surgical or traumatic "stress." The common initial signs in cases with rapid onset and with gradual onset are listed, together with the differential diagnoses that must be considered in the presence of these signs.

Particular attention is given to edema, which is presumed to occur as a result of the tendency to hypoproteinemia, hypernatremia, and vascular fragility. The effect of the syndrome on the metabolism of calcium and protein can become responsible for pathological fractures and renal calculus. Hypertension can become a continuous problem, even when the underlying cause has been adequately treated. The well-recognized susceptibility to infections in patients with Cushing's syndrome is reemphasized. Peptic ulcer occurred in 3 of the patients. The fact that the symptoms and signs in the neurological complications of Cushing's syndrome are similar to those in the Guillain-Barré syndrome and in diabetic neuropathy is discussed.

Report of an Outbreak of Bornholm Disease, with Isolation of Coxsackie B5 Virus: Toronto, 1958. D. E. Ryder, F. W. Doane, A. Zbitnew and A. J. Rhodes. Canad. J. Pub. Health 50:265-269 (July) 1959 [Toronto].

During an outbreak of epidemic myalgia or pleurodynia (Bornholm disease) in a Toronto suburb in 1958, a group of 16 families, comprising 27 cases of this disease, was studied. In only one family were all the members affected; in 3 others multiple cases occurred. The onset of the illness was usually acute, with temperatures up to 103 F and severe chest or/and abdomen pain. The duration was shorter in young children (about 7 days) than in older children and in adults (12 days). Complications (otitis media in one case, and mild bronchopneumonia in the other) occurred in 2 patients. Relapse occurred in 4.

Stool specimens were collected from all 27 patients and inoculated into monkey-kidney-tube culture. Virus was isolated from 21 of these specimens and identified as Coxsackie B5 in 20 strains and as Coxsackie B4 in one. Neutralizing tests were carried out on acute and convalescent serums from 10 patients who had excreted virus. The paired serums from 8 patients showed either a significant rise in, or a high level of, neutralizing antibodies in both serums. The high rate of isolation (78%) of Coxsackie B virus in this series and the results of the antibody studies, showing recent infection with the homologous virus in 8 of the 10 cases studied, confirm the results of other investigations concerning the role of Coxsackie B virus as an etiological agent in epidemic Bornholm disease.

The Mucocutaneous Lesions of Reiter's Syndrome. M. M. Montgomery, R. M. Poske, E. M. Barton and others. Ann. Int. Med. 51:99-109 (July) 1959 [Lancaster, Pa.].

Although the triad of urethritis, conjunctivitis, and arthritis (Reiter's syndrome) is now well known, the authors feel that the high incidence of mucocutaneous lesions is not generally appreciated. In their experience these mucocutaneous lesions occur so frequently in the endemic or venereal type of Reiter's syndrome, that this type might better be considered a tetrad, consisting in its complete form of urethritis, conjunctivitis, arthritis, and mucocutaneous lesions. The authors are chiefly concerned with the character and frequency of the mucocutaneous lesions and with their diagnostic importance. In the 38 patients with Reiter's syndrome treated during a 10-year period at the Hines

(Ill.) Veterans Administration Hospital, urethritis was recognized in all but 3, and these 3 had pyuria. Conjunctivitis was absent in only 5. Arthritis was the disabling component in all the patients. The authors feel that there is difficulty in the documentation of urethritis and conjunctivitis in patients seen a number of weeks after onset of the illness. In such cases, mucocutaneous lesions, which appear 4 to 6 weeks after appearance of the urethritis, may be the factor which establishes a definite diagnosis.

In the group of 38 patients, mucous membranes of the genitalia were affected in 30; mucous membranes of the mouth, pharynx, and tongue were affected in 14 of these 30. The skin was affected in 11 of the group. In no instance was the skin alone involved, and in no patient were oral mucous membrane lesions an isolated finding. Commenting on the mucous membrane lesions of the genitalia, the authors suggest that perimeatal erosions and balanitis circinata are probably of identical nature, and were present in all 30 of the 38 patients with mucosal lesions. Twenty-three had both lesions; 4 of the remaining 7 had perimeatal erosions, while the other 3 had balanitis circinata alone. The authors describe the morphology of the various genital lesions, of the buccal and pharyngeal lesions, and of the cutaneous lesions (keratosis of Reiter's syndrome).

The Influenza Epidemics of 1918 and 1957. M. Straub. Nederl. tijdschr. geneesk. 103:1208-1214 (June 6) 1959 (In Dutch) [Amsterdam].

The author reviews the literature on the 1918-1919 influenza epidemic and states that several groups of investigators searched for filtrable viruses and advanced the hypothesis of a specific influenza virus. He describes studies on 42 fatal cases of virologically confirmed Asian influenza that were observed in Rotterdam in 1957. These studies demonstrated the presence of 2 distinct types of the disease. The first type was characterized by secondary infection with Staphylococcus aureus, fatal aspiration pneumonia, and a peracute course of the disease; it was seen mainly in young women and children. The second type was marked by fatal virus pneumonia and developed in patients with chronic diseases of the heart and lung. During the winter influenza epidemics of the last 10 years, no virus pneumonia was seen, but staphylococcic influenza occurred. In 1918 streptococci and pneumococci played the same role as did staphylococci in 1957. In 1918 primary virus pneumonia also occurred in previously healthy persons, and became fatal as a result of secondary streptococcic and pneumococcic infections.

The author feels that pneumotropism of the virus and the nature of the secondary infection are both responsible for the virulence of influenza epidemics. The predisposition of young women to grave complications results from the relative narrowness of their tracheas. Pregnancy predisposes to virus pneumonia. The high incidence of fatal cases among elderly patients during influenza periods is due to existing respiratory infection and a tendency to thromboembolic processes.

Studies on the Origin of Drug-Resistant Staphylococci in a Mental Hospital. A. White, T. Hemmerly, M. P. Martin and V. Knight. Am. J. Med. 27:26-39 (July) 1959 [New York].

The authors studied the effect of antibiotics on staphylococci from 50 patients who were inmates of a mental hospital in Nashville, Tenn. Antimicrobial drugs had been used infrequently, and the staphylococci were largely susceptible. Nasal swabs were taken regularly, beginning in October, 1957, and were continued through August, 1958. The patients were given courses of treatment with erythromycin, penicillin, and tetracycline in order to judge the effect of these agents on various aspects of the staphylococcic carrier state. Erythromycin, to which all cultures before treatment were susceptible, caused a complete suppression of the carrier state, and only a few resistant strains appeared subsequently. Penicillin, to which 10% of strains were resistant before treatment, caused a drop in the carrier rate to 60%, but the fall was limited at this point by an increase in strains resistant to penicillin. Tetracycline, to which 4% of strains were resistant before treatment, caused a fall in carrier rates to 20%, at which point increase in resistant strains prevented further reduction. After treatment, the carrier rates in treated patients increased, and the frequency of resistant strains diminished. Treated noncarriers and nontreated carriers on the same ward did not change during therapy experiments. Successive treatment of patients with penicillin and tetracycline caused the appearance of a group of cultures resistant to both penicillin and tetracycline, of which a majority did not react with phage (no type). A high proportion of strains of phage type 52-80 susceptible to penicillin and tetracycline, initially present on the ward, completely disappeared after use of these agents.

Clinical Characteristics of Leptospirosis: Observations Based on a Study of Twelve Sporadic Cases. G. A. Edwards. Am. J. Med. 27:4-17 (July) 1959 [New York].

A study of 12 sporadic cases revealed leptospirosis to be an acute, self-limited, diphasic illness with a low incidence of jaundice or significant renal damage. In the majority of cases the onset of illness was abrupt. All the patients had fever and chills, and most of them had minor gastrointestinal complaints. Since Leptospira organisms can be recovered from the blood and cerebrospinal fluid during this first phase in a high percentage of cases, it has been designated as the "septicemic" stage. The second stage begins as defervescence, and symptomatic improvement occurs on the 6th or 7th day. Shortly after the end of the first stage there is usually a secondary rise in temperature and development of meningitis, either asymptomatic or clinical. It has been demonstrated repeatedly that the blood and cerebrospinal fluid are sterile during this stage, organisms rarely having been recovered after the 7th or 8th day. During this second stage antibodies appear in the blood in rapidly rising titer. In addition to fever and meningitis, several infrequent manifestations, such as iridocyclitis and various neurological lesions, may develop. It is proposed that this phase be designated as the "immune" stage, since manifestations are primarily due to hypersensitivity. Not all the patients had overt meningitis. Three patients had pleocytosis without any of the usual signs or symptoms of meningitis. Another patient had severe delirium, beginning on the 6th day, and, although he had pleocytosis, he was not considered to have clinical meningitis.

It was impossible to correlate the different clinical disease patterns with the leptospiral serotypes identified in these cases. There are no clinical syndromes exclusively linked with infection by specific serotypes; nor are there any serotypes which always cause the same pattern of disease. For this reason the use of special names as synonyms for infections with certain species is not justified. The diagnosis of leptospirosis should be considered in any patient with an acute illness characterized by headache, myalgia, fever, chills, and conjunctival suffusion, and in any patient in whom "aseptic meningitis" develops after an acute febrile illness of 5 to 7 days' duration. The greatest danger of infection in man is from contact with stagnant water to which wild or domesticated animals have access, but infection may result from direct contact with the urine of infected animals as well.

SURGERY

Congenital Heart Disease: III. Coarctation of the Aorta. C. J. O. Brown, B. L. Deans, J. M. Gardiner and others. M. J. Australia 1:857-864 (June 27) 1959 [Sydney].

The authors report on 100 patients (68 male and 32 female), between the ages of 4 months and 56 years, with congenital coarctation of the aorta, seen at the Alfred Hospital in Melbourne, Australia. An attempt at surgical correction was made in 74. Two patients, a 24-year-old woman and an 8-year-old girl, proved to have inoperable disease; the adult had a narrowing of the whole length of the thoracic aorta with extensive calcification, and the child had associated patent ductus arteriosus and a large aortopulmonary septal defect. In 72 patients excision of the constricted area of the aorta was performed with the aid of anesthesia, which was induced with thiopental (Pentothal) sodium and curare after insertion of an endotracheal tube. Anesthesia was continued with nitrous oxide and oxygen, with fully controlled respiration. Trimethaphan (Arfonad) camphorsulfonate was used in 30 patients to induce hypotension; administration of the drug was started before the incision was made and was maintained until completion of the anastomosis, when the blood pressure was allowed to rise slowly. In most of the patients the blood pressure was reduced to 80 to 100 mm. Hg from the start of the operation.

Of the 72 patients, 5 died as a result of the operation. Of the 67 patients operated on successfully, the continuity was restored by an end-to-end anastomosis in 65; in 2 the subclavian artery was divided and turned down and anastomosed to the descending aorta. In 6 patients arterial homografts were used. Of the 67 patients, 6 had a normal blood pressure before the operation. In 48 of the remaining 61 patients, the blood pressure in the upper extremities was reduced to below 140/90 mm. Hg, with a corresponding rise in the femoral artery pressure. Three of these patients died subsequently. In 11 patients the blood pressure was reduced, but not to normal. Five of these had aortic regurgitation in addition to their coarctation, and 1 of these 5 required a graft. There were 2 patients in whom the blood pressure was not reduced; one of these had aortic incompetence in addition to coarctation.

The authors believe that most of the patients with coarctation of the aorta should be operated on. The best time for the operation is considered to be between the ages of 8 and 15 years, but it may be performed earlier if there is evidence of cardiac strain or severe hypertension. Most patients, aged less than 30 years, should be operated on, and one should not hesitate to operate on those above this age if the coarctation is producing symptoms, but operation is not indicated in the terminal stages of cardiac breakdown. Aortic incompetence is not a contraindication to operation, but may vitiate the result. Aortic stenosis does seem to be a contraindication unless it can be relieved at the same time or later. Hypotension induced with trimethaphan is a valuable adjunct to the operation. Interrupted sutures, with 00000 arterial silk, should be used for the anastomosis. The results of surgical treatment have proved gratifying.

Surgical Treatment of Recurrent Fibroadhesive Cerebellomedullary Arachnoiditis. J. B. Albertengo. An. cir. 24:1-11 (Jan.-March) 1959 (In Spanish) [Rosario, Argentina].

A new operation is described, aimed at reestablishing the circulation of the cerebrospinal fluid in patients with blockage of the subarachnoid space due to severe forms of recurrent fibroadhesive cerebellomedullary arachnoiditis. The procedure consists in placing 1 or 2 catheters over the blocked segment of the subarachnoid space, establishing communication between the lateral ventricle, the cisterna magna, and the subarachnoid space at the level of the 5th, the 6th, or the 7th cervical vertebra according to the extension of the arachnoiditis. The ends of the catheters are sutured. The lower ends are introduced in the subarachnoid space of the cervical canal by removing half of a vertebral lamella and making a hole in the dura mater. The catheters are of rubber or polyethylene.

Four representative cases are reported. In the 4 patients decompression and liberation of adhesions gave temporary relief, followed by reappearance and aggravation of the neurological symptoms and a progressive course of the disease. In 2 patients the blockage caused by the arachnoiditis involved mainly the cisterna magna and the posterior fossa. These patients were cachectic for 3 months and in a coma for the last week preceding the operation. Two catheters were placed, one from the lateral ventricle to the cisterna magna, and the other from the cisterna magna to the cervical subarachnoid space. The patients were in normal health, without any signs of intolerance to the catheters, 10 and 4 years, respectively, after the operation. In the only child in this series, a 6-month-old infant, the posterior fossa was blocked. The catheter was placed from the lateral ventricle to the cisterna magna and the subarachnoid space under the 4th cervical vertebra. At the age of 3 years the child had normal height and weight, but did not walk, and spoke only a few words. The 4th patient had acute neurological symptoms, mainly paralysis of the legs and impotence. A neurinoma was surgically removed from the spinal canal without relieving the neurological symptoms. An operation performed 2 years later showed an enormous mass of fibroadhesive tissue which filled the spinal canal and the cauda equina. After removal of the fibroadhesive tissue, 2 catheters were placed in the subarachnoid space, one from the 12th to the 6th thoracic vertebrae, and the other from the 10th to the 3rd. The catheters in this case had perforations at 1-cm. intervals. There was a marked but temporary improvement, followed by reappearance of the neurological symptoms, including paralysis of the legs and impotence.

Occlusive Disease of the Carotid Arteries. A. Silverstein. Circulation 20:4-16 (July) 1959 [New York].

Occlusions of the carotid arteries may be responsible for more than 20% of all acute cerebral vascular lesions. The author reports on the clinical features of 50 hospitalized patients, ranging in age from 26 to 82 years, with occlusive disease of the carotid arteries. Thirty-seven patients were males, and 13 were females. There were 28 occlusions in the right carotid artery and 20 in the left carotid artery and 2 instances of bilateral complete carotid occlusion. There was evidence of vascular lesion elsewhere in the body in 38 patients. The onset of symptoms was sudden in 36 patients and gradual in 14. Motor weakness was the commonest neurological finding, hemiparesis or hemiplegia being present in 49 patients. Carotid arteriography was performed in 47 instances; the clinical course of only 2 patients tended to progress immediately after arteriography. Transient neurological deficits after angiography of the patent carotid artery developed in 2 patients and lasted less than 24 hours.

Anticoagulant therapy was given to 14 patients; neck surgery was performed on 6; and trypsin was administered intramuscularly to 1. Seventeen patients showed a moderate neurological improvement and have maintained it. Ten patients have died, probably because of carotid occlusion. Moderate to severe degrees of atheroma formation were observed in most of the 10 specimens (6 surgical and 4 autopsy) of carotid arteries studied. The results of therapy are not presented, because the number of patients was small and the follow-up periods were brief. It is not yet known which form of therapy, anticoagulant or surgical, is to be preferred. The diagnostic methods for determining carotid occlusion, which were used in this series with significant regularity, were ophthalmodynamometry and carotid compressions. Definitive diagnosis requires arteriographic study.

Acute Pericardial Fat Necrosis: Report of a Case. M. H. Chester and J. B. Tully. J. Thoracic Surg. 38:62-66 (July) 1959 [St. Louis].

The pericardial fat necrosis syndrome was first recognized as a clinicopathological entity by Jackson, Clagett, and McDonald in 1957, when they reported 3 cases in which exploratory thoracotomy was performed from 7 to 10 weeks after the acute onset of symptoms. These investigators emphasized that acute pericardial fat necrosis can simulate acute myocardial infarction, pulmonary embolism, or hemorrhage into a neoplasm of the lung. The roentgenographic appearance may easily be misinterpreted as a primary or metastatic carcinoma of the lung, a localized pleural effusion, pleuropericardial cyst, or mesothelioma. A consideration of this disease entity is, therefore, warranted in any patient with unexplained precordial pain, pleuritic pain in the lower chest on the left, and an associated juxtacardiac mass.

The authors present a 46-year-old man who during a severe lifting effort experienced the sudden onset of anterior chest pain and cramping epigastric pain. The pain radiated to the left shoulder and increased on deep inspiration; it became excruciating and caused syncope. The patient was hospitalized 3 days after the onset of the pain, with diagnosis of acute myocardial infarction. He was pale, sweating, and had excruciating chest pain; respirations were rapid and shallow; blood pressure, 98/68 mm. Hg; and pulse, 126. He was unable to take a deep breath because of the exacerbation of the chest pain. Auscultation elicited normal breath sounds. An unusual, soft, low-pitched rub, however, was heard during expiration. This sound resembled the sound produced by compressing a wet sponge. It could easily be distinguished from the classical friction rub of a pericarditis. The rub disappeared on the third hospital day. An electrocardiogram was normal, except for an occasional ventricular presystole. Chest roentgenograms demonstrated a juxtacardiac mass along the anterior aspect of the left cardiac border; tomograms of the juxtacardiac mass revealed several ovoid areas of decreased density. Serial electrocardiograms and serum transaminase determinations were normal.

An exploratory operation was performed on this patient 13 days after the acute onset. A firm ovoid mass, measuring 10 by 7 cm., was identified as the pericardial fat pad. It was adherent to the anterior and lateral aspect of the pericardium and the anterior chest wall. There were also adhesions binding the lingula to the pericardial fat pad. The mass was excised by lung dissection. Histological studies on the removed tissues revealed that the changes were due to extravasation of blood, ischemic fat necrosis, and fibrosis. Moderate endarteritic changes were also noted. A traumatic etiology is a strong probability in this case.

The Clinical Evolution of Shunt-Operations for Morbus Caeruleus: Results of 150 Operations, in a Long-Term Follow-Up. C. A. Mahaim, C. L. C. van Nieuwenhuizen, H. A. D'heer and F. Slooff. Am. Heart J. 58:13-25 (July) 1959 [St. Louis].

The aim of the operations of Blalock, Potts, and Brock, used in treating the tetralogy of Fallot, is to augment the pulmonary circulation in order to increase the oxygenation of the blood. They do not correct the malformation; in fact, with the procedures of Blalock and Potts, a 5th malformation is created in a heart that already has 4. An operation which creates an artificial ductus arteriosus must, in the long run, produce overloading of the heart, but the immediate benefits of the operation, insofar as the general status of the patients and the amelioration of the cyanosis are concerned, are so evident that the usefulness of this type of operation is universally recognized. But what is the future of these patients? The authors investigated the long-term results in 141 patients subjected to 150 operations between 1948 and 1956 at the St. Antonius Hospital, Utrecht, The Netherlands. The Potts procedure was performed 88 times; the Blalock method, 42 times; the procedure of Brock, 17 times; exploratory thoracotomy, once; and 2 patients died under anesthesia before the operation was begun. In 9 of the 141 patients a second operation was performed. All living patients except one were reexamined in 1956 or 1957.

A preoperative prognosis had been made, taking into account such factors as age, hemoglobin content, electrocardiogram, and roentgenogram. The following were the most important factors that adversely influenced the prognosis: (1) the detection of malformations not corresponding to those characteristic of the tetralogy of Fallot; (2) electrocardiographic indications of a left or an extreme right ventricular hypertrophy; (3) age younger than 2½ years or older than 17 years; (4) a cardiothoracic ratio of 55% or more; (5) a hemoglobin value of more than 150% or less than 70%; (6) body weight of more than 10% below normal; and (7) presence of signs of circulatory deficiency at birth.

Patients were divided into 3 groups with regard to the aforementioned criteria. Group 1 included the patients with a good prognosis, that is, none of the 7 adverse factors were present. Group 2 included the patients with an average prognosis, one of the adverse factors being present. Group 3 included the patients with a poor prognosis because from 2 to 6 of the adverse factors were present. Of the patients who had a favorable preoperative prognosis, 90% obtained good results, one-third of which were excellent; the mortality in this group was 4%. In the patients with an unfavorable preoperative diagnosis, the mortality was 10 times greater. The favorable results obtained with the 3 operations persisted during the years following. In general, the postoperative modifications in the clinical signs, the electrocardiograms, and the roentgenograms were stabilized within the first 2 years after the operation. Some patients, even after a period of several years, had normal cardiac function, as indicated by a cardiac function test.

The optimal size of the operative shunt ranges from 4 to 6 mm. in diameter. The best results are obtained with the Potts and Blalock procedures; the Brock operation should be avoided because of a high operative mortality, probably as a consequence of the frequency of the infundibular type of stenosis in the tetralogy of Fallot.

Thrombosis of the Inferior Vena Cava. A. Buzzi, O. Fustinoni, T. J. Gutierrez and H. A. Ruggiero. Rev. Asoc. méd. argent. 73:189-195 (June) 1959 (In Spanish) [Buenos Aires].

The clinical polymorphism presented by thrombosis of the inferior vena cava may constitute a serious diagnostic problem. Besides the easily recognized cases in which a thrombophlebitis of the lower extremities extends into the iliac veins and occasionally into the inferior vena cava, there are cases in which a caval thrombotic obstruction develops without any warning signs or symptoms. Sometimes it constitutes a terminal, asymptomatic stage which is diagnosed only at autopsy. The authors report on 5 cases that illustrate the incidence of insidious development and the potential danger of an unrecognized inferior caval thrombosis.

In the first case the patient was a 26-year-old man whose earliest symptom was sudden, continuous, and severe lumbar pain. Primary thrombosis of the inferior vena cava developed, together with deep collateral circulation. After 45 days, during which the course of the disease showed steady aggravation, ligation of the inferior vena cava was performed. One year later the patient still had edema of the lower extremities and a scant peripheral collateral circulation, but the over-all clinical picture indicated that his disease had been arrested. The second patient (a 57-year-old man) was hospitalized because of phlebothrombosis of the lower limbs. Later signs of pulmonary embolism developed, but ligation of the inferior vena cava was considered inadvisable, and the patient died approximately 3 months after hospitalization. In the case of the third patient (a 38-year-old man) the inferior caval thrombosis, complicating a bacterial endocarditis, was not discovered until autopsy. The fourth and fifth patients were 2 men, aged 51 and 54 years, respectively, who were suffering from thrombophlebitis and whose disease, after an interval of 10 years in one case and of 6 months in the other, developed into inferior caval thrombosis.

The authors stress the need for alertness to the possibility of caval thrombosis even in the absence of any signs or symptoms, and recommend the use of cavography with the purpose of confirming the diagnosis and evaluating the deep collateral circulation. From the therapeutic point of view, they recommended the administration of anticoagulants, to avoid repetition of the thrombotic accidents, and the surgical ligation of the vena cava, to avoid the ascending extension of the thrombosis.

GYNECOLOGY & OBSTETRICS

Early Endometrial Carcinoma Following Prolonged Estrogen Administration in an Ovariectomized Woman. Y. M. Bromberg, E. Liban and A. Laufer. Obst. & Gynec. 14:221-226 (Aug.) 1959 [New York].

The authors report on a 42-year-old woman in whom an early endometrial carcinoma developed after bilateral ovariectomy which had been performed 24 years previously for torsion of an ovarian cyst. The patient had been treated for continued vasomotor disturbances with estrogens during the entire period after the operation, and a total amount of 9.2 Gm. of estrogenic substances had been administered. Fairly considerable uterine bleeding took place. An endometrial biopsy revealed glandular cystic and adenomatous hyperplasia of the uterus and early carcinoma. Total hysterectomy was performed. The postoperative course was uneventful, and when the patient was last seen, 24 months after the hysterectomy, her general condition was satisfactory, and no evidence of metastasis was found. It was noted that the patient's mother had died of carcinoma of the uterus. A synergistic effect of prolonged estrogen therapy and of a hereditary predisposition to the development of the carcinoma is suggested as a possible explanation for the appearance of the tumor in this patient.

Morbidity and Mortality of Total Abdominal Hysterectomy and Late Results in Patients Operated on for Nonmalignant Diseases of the Uterus. R. Bianco and F. Di Re. Tumori 45:189-200 (March-April) 1959 (In Italian) [Milan, Italy].

The authors report on a study of the morbidity and mortality and late results in a group of 107 women on whom total abdominal hysterectomy for both malignant and benign disease of the uterus was performed at the Cancer Institute of Milan during 1954-1958. All the patients survived the operation. Two instances of a vescicovaginal fistula and one of an ureterovaginal fistula were the only complications of the operation. A 48-year-old woman, operated on for adenocarcinoma, and a 58-year-old one, operated on for myoma of the uterus, both presenting varices of the lower limbs, developed phlebitis from which, however, they recovered. A 67-year-old patient in poor general condition, operated on for adenocarcinoma, suffered on the 8th postoperative day from eventration which required emergency suturing. Five patients developed cystitis, which most likely was caused by the use of a catheter during the first 24 hours after the operation; this condition disappeared rapidly. The neck of the uterus was free from alterations in only 30 of the 107 patients; a hyperplasia of the basal strata of the epithelium of the portio was observed in 23 instances. Cancer of the neck of the uterus was present in 11 patients.

Late results from follow-up examinations were gathered in only 70 of the 107 cases; some patients could not be reached, and those operated on during the second semester of 1958 were not considered. None of the 70 patients presented alteration in the state of the pelvis. Five patients were suffering from dyspareunia, one of them suffering from this condition even before the operation. One patient, 65 years of age, presented a shortened vagina. The authors point out that this finding would have been more frequent had they not, in performing the hysterectomy, resected the vagina at the point where the fornices become inserted in the neck of the uterus. The libido increased in 6 patients and declined in 5. Seven patients presented a granuloma in the fundus of the vagina, but this was easily removed in each instance. Three patients presented incontinence of urine, and 2 presented frequent episodes of cystitis.

The authors believe that total abdominal hysterectomy is the operation of choice in patients with nonmalignant diseases of the uterus, when in these patients it is not possible to perform another type of operation that could retain the function of the uterus. Total hysterectomy is to be preferred to subtotal hysterectomy—first, because the risk incurred in both operations is the same, and, second, because the high incidence of pathological manifestations connected with residual stumps after subtotal hysterectomy can be eliminated by total hysterectomy.

Foetal Wastage in Twin Pregnancy. S. H. Tow. J. Obst. & Gynaec. Brit. Emp. 66:444-451 (June) 1959 [London].

The author reports on 408 women with twin pregnancies, who were admitted to the Royal Maternity Hospital in Belfast for delivery between 1947 and 1956. Of the 816 infants, 3 first twins were born at home, and the remaining 813 infants were born in hospital. There were 51 stillbirths (6.3%) and 49 deaths in the first week of life (6%), making a total fetal loss of 12.3%. While this figure is high, it compares favorably with the best results obtained by other workers. Antenatal, intranatal, and postnatal risks of twin pregnancy, in large measure associated with gross prematurity, contribute to this high mortality. By comparing the incidence of preeclampsia, premature deliveries, and vertex-vertex presentation in the patients who had registered for antenatal care with that in those who did not, it appeared that antenatal care and bed rest in hospital conferred striking benefits in reducing maternal complications and prolonging gestation, thus leading to a reduction in prematurity and fetal wastage. Accurate diagnosis and careful antenatal supervision are essential in women with twin pregnancies. In order to prevent onset of premature labor, bed rest in hospital from the 30th week is suggested. Only 137 (33.5%) of the 408 women were delivered of both infants spontaneously. The need for operative assistance in the remaining 271 (66.5%) patients makes it imperative for all women with twin pregnancies to be confined in hospital. The second twin is specially susceptible to perinatal death on account of labor hazards arising from malpresentation and disturbed uteroplacental circulation after the birth of the first twin. In order to reduce the risk of such death, rupture of the membranes within 10 minutes, followed by prompt and skilled delivery, is advocated.

PEDIATRICS

Seasonal Aseptic Meningitis Caused by Coxsackie and Echo Viruses, Toronto, 1957. M. Clarke, M. Hunter, G. A. McNaughton and others. Canad. M. A. J. 81:5-8 (July 1) 1959 [Toronto].

The increasing use of tissue culture methods has clarified the etiology of aseptic meningitis to a great extent. It is now evident that except in a poliomyelitis epidemic the virus of poliomyelitis plays a minor role in the etiology of aseptic meningitis. Between June and October, 1957, a total of 65 children were admitted to the Hospital for Sick Children, Toronto, with a diagnosis of aseptic meningitis. Of these cases, 51 were chosen for special study; the clinical diagnosis was confirmed by the finding of characteristic changes in the cerebrospinal fluid. The majority of cases occurred in July and August, and the males outnumbered the females 2:1. Seventeen patients (33%) were less than 4 years old, and the others ranged in age from 5 to 14 years. The illness was acute in the majority of patients, commencing 1 to 3 days before admission. The symptoms were those typical of the aseptic meningitis syndrome. Five patients presented with a rubelliform rash similar to that found in 1956 associated with infection by enteric cytopathogenic human orphan (ECHO), type 9, virus. Splenomegaly was noted in 7 cases. Cells were present in the cerebrospinal fluid in all the patients, the count ranging from 25 to 1,600 cells per cubic millimeter. The mean figure of 400 cells per cubic millimeter was much higher than that usual in poliomyelitis. The cells were mainly lymphocytes. Patients in whom the cell count was more than 500 cells per cubic millimeter were all infected with ECHO viruses. White blood cell counts were normal or slightly elevated. All the children were seen 2 to 8 weeks after discharge. Apart from a few who tired easily, all had completely recovered.

A variety of agents were found responsible for the illnesses. Distinctive were the cases of rubelliform rash in association with the aseptic meningitis syndrome. ECHO, type 9, virus was the agent chiefly associated with cases of rash, although one such case yielded an unidentified ECHO virus. From the total of 51 cases, 36 viruses were isolated by inoculation of human amnion or monkey kidney cells. Viruses were identified as belonging to the following established types: Coxsackie A9, B3, B5, and ECHO, types 6 and 9. Fifteen strains were unidentified but could be allocated provisionally to 3 groups: 9 unidentified ECHO viruses, 4 Coxsackie A viruses, and 2 strains of mumps virus. Serologic evidence combined with the results of tests on blood and cerebrospinal fluid suggested that the stool isolates were active agents in the meningitis syndrome. Thus, of the total 51 cases, 48% were due to ECHO viruses, and 18% to Coxsackie viruses. An additional 14% were established on serologic grounds as due to mumps. The remaining 20% of the cases, yielding no evidence of infection with enteric viruses or mumps, provide a problem for future studies.

The Behavior of the Red Blood Cell Count and the Value of Hemoglobin During the First Semester of Life in Infants Subjected to Exchange Transfusion. W. Felici and G. Di Piero. Policlinico (sez. prat.) 66:825-829 (June 15) 1959 (In Italian) [Rome].

The red blood cell count and the hemoglobin values were checked periodically for 6 months in 20 newborn infants, 13 of whom had suffered from incompatibility in the Rh system and 7 from incompatibility in the ABO system. Each infant had received an exchange transfusion of 500 cc. of blood. The increase of red blood cells was slow and very irregular in each case. The average count at the first control after the blood transfusion was 3,740,000 per cubic millimeter (with 3,000,000 and 4,740,000 as extreme values); at the last count, 6 months later, the average count had gone up to 4,000,000 per cubic millimeter (with 3,500,000 and 4,940,000 as extremes). Changes in the hemoglobin values were not significant. A severe anemia was noticed during the second and third months of life in 4 infants; this crisis was coincident with the so-called physiological anemia of the newborn. Treatment with liver extracts and vitamin B_{12} gave good results even in infants with the severest forms of anemia. The authors believe that the first 6 months of life in an infant who has had hemolytic disease and who has been treated with exchange transfusion represent a critical period for restoring the normal blood picture. It is especially important to control for some time the red blood cell count, even if this count returns to normal right after the transfusion, and to check with adequate treatment any eventual irregularities.

Hyperbilirubinemia in Premature Infants: A Follow Up Study. C. A. Koch, D. V. Jones, M. S. Dine and E. A. Wagner. J. Pediat. 55:23-29 (July) 1959 [St. Louis].

Serial determinations of serum bilirubin values were made during the first week of life in 100 premature infants. None of the patients had any demonstrable evidence of infection or isoimmunization. Those who developed hyperbilirubinemia were considered to have "physiological jaundice," and at that time (1953) no treatment was instituted. Eight infants died, 2 of them having had kernicterus; their bilirubin levels had been greater than 20 mg. per 100 ml. The remaining 6 infants, who died of other causes, had bilirubin levels below 20 mg. per 100 ml. Of the surviving infants, none had neuromuscular abnormalities on discharge from the nursery. Forty-nine infants were followed up at the age of one year or more; 5 of these had neuromuscular abnormalities highly suggestive of kernicterus. All these patients had had serum bilirubin levels of more than 20 mg. per 100 ml. during the neonatal period. The relation of kernicterus to birth weight and condition of the infants at birth was not so distinct as the relation to hyperbilirubinemia. The difficulties encountered in establishing a clinical diagnosis of kernicterus in the first weeks of life make repeated follow-up examinations of the infants over a period of several years necessary. Exchange transfusions are indicated for all infants with hyperbilirubinemia during the neonatal period if it is evident that the serum bilirubin levels will exceed 20 mg. per 100 ml.

Problems Presented by the Jaundiced Newborn. C. M. McCue, A. B. Mayer and R. O. Hudgens. Virginia M. Month. 86:390-395 (July) 1959 [Richmond].

One hundred sixty-one of the 6,085 infants who were born in, or admitted to, the hospitals of the Medical College of Virginia in Richmond during 1957 developed significant jaundice in the neonatal period. Eighty of the 161 infants were white and 81 were Negroes; 73 were male and 88, female. The birth weight of 158 of the 161 infants ranged from 1,000 Gm. for the smallest infant in the series to 4,250 Gm. for the largest; approximately 30% of the total group were of a weight less than 2,500 Gm., which was considered premature for the purpose of this study. Jaundice was thought to be of physiological origin in 103 infants; icterus was detected within 36 hours after birth in 20 of these infants and during the first 24 hours of life in 6. Thirteen of the 76 jaundiced infants in whom bilirubin was determined presented a maximum bilirubin level in excess of 20 mg. per 100 cc. None of the 103 infants received replacement transfusion. Only one death occurred in this group of infants.

Thirty-nine infants showed jaundice in association with erythroblastosis due to either Rh or ABO incompatibility. The generally accepted methods of treatment with replacement transfusions gave satisfactory results in 17 instances. In this group only 2 babies with a severe form of the disease died. On autopsy one of them was proved to have kernicterus; the total bilirubin level never exceeded 16 mg. per 100 cc., but the infant presented hypoxia.

Jaundice was due to sepsis in 20 instances. Blood cultures were taken in each case, but a positive bacteriological isolation was obtained in only 5 infants. Findings, such as unstable temperature curve, lethargy, anorexia, abdominal distention, and failure to gain weight, when combined with visible jaundice, according to the authors, justify the diagnosis of sepsis despite the lack of bacteriological proof. Thirteen of the 20 infants were of premature weight. Jaundice was detected from 36 hours to

26 days after birth. Seven infants of this group, 6 of premature weight, died despite antibiotic therapy, maintenance of fluid and nutritional requirements, and general and supportive care. Two of these infants were moribund on arrival at the hospital and died within 9 hours of admission.

Congenital Leukemia. M. A. Brescia, E. Santora and V. F. Sarnataro. J. Pediat. 55:35-41 (July) 1959 [St. Louis].

The authors report on a fatal case of congenital stem-cell leukemia in a 28-day-old boy. The infant was apparently well when born after an uncomplicated labor, the birth weight being 7 lb. 6 oz. (3,345 Gm.), and he gained weight normally until the 28th day of life when he refused his feeding. Thereafter his condition deteriorated rapidly, and he died 2 hours after admission to the hospital, despite oxygen and other supportive treatment. A blood count obtained before death revealed 1.5 million leukocytes per cubic millimeter. Autopsy showed that all the hemopoietic, as well as the nonhemopoietic, organs were markedly infiltrated with leukemic cells. The mother's history revealed that she was subjected to repeated roentgenologic examinations 5 months before the beginning of gestation. A marked increase has been reported in the incidence of leukemia and other types of neoplasms in children during the first 10 years of life when their mothers have received diagnostic examinations during pregnancy. Whether roentgen radiation received before pregnancy is an etiological factor requires further study and observation.

Eosinophils in the Thymus in Hyaline Membrane Disease (Respiratory Distress Syndrome). M. M. Black and A. G. Baldi. Pediatrics 24:205-214 (Aug.) 1959 [Springfield, Ill.].

Hyaline membrane disease was found to be commonly associated with perivascular aggregates of mature and immature eosinophils in the septums of the thymus in premature infants. Similar eosinophilic aggregates were much less frequent in the thymus glands of stillborns and in cases of perinatal death in which the infants had no hyaline membrane disease. Among 27 infants with hyaline membrane disease, 20 (74%) had both mature and immature eosinophilic aggregates, grading 4 plus or more. This degree of eosinophilia was found in only 2 (6%) among 35 cases of stillbirths and of perinatal deaths in which the infants had no hyaline membrane disease. Hyaline membrane disease was found in 27 (53%) of 51 cases of perinatal death, the infants weighing between 850 and 3,500 Gm. (about 2 and 8 lb.). However, hyaline membrane disease occurred in 20 (87%) of 23 cases of perinatal death in which the infants had thymic eosinophilia; in contrast, among similar cases but without eosinophilia, hyaline membrane disease occurred in only 7 (25%) of 28 infants. These data suggest that the frequency of eosinophilia was significantly greater in infants with hyaline membrane formation than in those without it.

The occurrence of eosinophilia in the thymic septums of infants with hyaline membrane disease could not be explained by either birth weight or duration of postnatal survival. Numerous eosinophils were also found in the axillary lymph nodes in 4 of 8 cases of hyaline membrane disease. Further investigation is needed to elucidate the participation of various vascular homeostatic mechanisms in the pathogenesis of this condition, such as adrenal steroids and proteins in the serum and lymphoreticuloendothelial system. Such an approach might yield information of therapeutic as well as academic value.

Clinical Observation of Familial Phenylpyruvic Oligophrenia. L. Yasse. Acta paediat. belg. 13:86-102 (no. 2) 1959 (In French) [Brussels].

The author reports the familial occurrence of phenylketonuria (phenylpyruvic oligophrenia) in 2 girls, aged 12 and 10 years, who were sisters, and in a 9-year-old girl, who was a second cousin of the 2 sisters. Three living siblings of the sisters were completely normal. The sisters both had ash-blond hair and showed the classic manifestations of phenylketonuria, namely, a dry, rough, and scaly skin, jerky movements of the extremities, and a low-grade intelligence, their intelligence quotients being 40 and 70 respectively. Both these children excreted phenylpyruvic acid in the urine, and chromatography revealed excessive amounts of phenylaminopropionic acid (phenylalanine). The sisters' cousin had 6 normal siblings; she too had ash-blond hair and a dry, rough, and scaly skin; her face was inexpressive; her lower extremities were cyanosed and cold and habitually held in flexion. Her mental defect was similar to that of the older of the 2 sisters, but repeated examination of the urine did not reveal the presence of phenylpyruvic acid. The clinical aspect of this third patient thus was typical of phenylketonuria, but the biochemical aspect was not. Early placement of such patients with phenylketonuria on a phenylalanine-deficient diet is emphasized.

UROLOGY

Unilateral Renal Artery Disease with Hypertension. J. J. Cordonnier. J. Urol. 82:1-9 (July) 1959 [Baltimore].

Recent advances in vascular surgery have produced increased interest in unilateral renal artery disease as an etiological factor in hypertension. During the past 2 years the author had occasion to follow 7 patients in whom the diagnosis of hypertension secondary to unilateral renal artery disease seemed authenticated, and in whom nephrectomy produced a satisfactory clinical response. One of the cases presented falls into the category of congenital narrowing of the renal artery; 2 presented classical partial renal infarction; 1 was secondary to trauma; and the other 3 were secondary to atherosclerosis. In order to produce hypertension, renal ischemia with relatively normal parenchyma is necessary. Intravenous pyelography is of definite value as a screening procedure in all cases of hypertension, and the presence of decrease in size and/or function on one side may be significant. However, this finding alone is not sufficient basis for nephrectomy.

Two cases demonstrated clearly the danger of depending on intravenous pyelography alone. In both cases the dye concentration, adequate on both sides, was, if anything, somewhat better on the affected side. In cases of this type, aortography is an absolute necessity prior to surgery. Furthermore, normal intravenous pyelograms do not rule out the possibility of unilateral vascular disease. The use of differential sodium studies and volume of urine excretion is of value as a screening procedure but must be substantiated by aortography. In patients with a fairly typical history of renal infarction, or in whom there is no excretion of dye on the affected side with normal retrograde filling of calyces and pelvis, aortography is not necessary to establish the diagnosis of unilateral arterial disease, and since aortography is not without a certain degree of hazard, the author does not use it under these circumstances.

The author feels that unilateral renal vascular disease has not received sufficient attention from urologists in the past. The results in the cases presented have certainly been gratifying and should stimulate a more careful evaluation of all hypertensive patients. On the other hand, careful and thorough evaluation must be performed in each individual case, if unnecessary and unwise nephrectomy is to be avoided in some instances.

Hypernephroma Associated with Polycythemia. J. H. De Weerd and A. B. Hagedorn. J. Urol. 82:29-36 (July) 1959 [Baltimore].

Anemia ranks high on the list of common clinical findings associated with hypernephroma. Hence it would appear somewhat incongruous to associate in a cause-effect manner the antithesis of anemia, polycythemia, with the same lesion. Personal experience with 3 such cases prompted further search, and records of 7 well-documented cases were found in the Mayo Clinic files for the past 10 years. The authors have found it difficult to identify the polycythemia in these patients as either polycythemia vera or secondary polycythemia. None of the patients had leukocytosis, thrombocytosis, or splenomegaly on initial examination. The clinical response to nephrectomy appears to offer formidable supportive evidence to the diagnosis of secondary polycythemia in 5 of the 6 patients who survived operation. These 5 patients experienced remission of their polycythemia for periods ranging from 9 months to 5½ years. Two of the 5 experienced apparent exacerbation when metastasis became clinically evident, and the 6th patient, whose polycythemia was less favorably affected, had pulmonary metastasis at the time of nephrectomy.

The etiology of this form of secondary polycythemia remains a matter of conjecture. The size of several of the tumors in these patients is noteworthy, as is the fact that in 4 of the 7 patients special mention was made of huge dilatation of the veins, over and above the normally anticipated vascularity of renal adenocarcinomas. These facts seem to give credence to theories that rapid shunting of arterial blood to these dilated veins leads to increased erythropoietic activity. Jacobson and co-workers in 1957 postulated the role of the kidney in active erythropoiesis as that of either producer or activator of erythropoietin. Renal tumors, then, may produce an excess of these factors. One can postulate exacerbation of increased erythropoiesis coincident with development of metastatic lesions after nephrectomy.

Novobiocin-Sulfamethizole Combination in the Treatment of Genitourinary Infections. J. M. Costa and M. Stella. Hospital, Rio de Janeiro 55:79-83 (June) 1959 (In Portuguese) [Rio de Janeiro].

The problem of primary or secondary genitourinary infection, one of the most complex in urology, has been further complicated by the development of bacterial forms resistant to antibiotic therapy. Among the new preparations aimed at solving this problem is the combination of novobiocin and sulfamethizole, which the authors used in treating 82 patients, whose ages ranged from 5 to 86 years. In 62 patients the genitourinary infection was primary; in 20 it was secondary, following a surgical intervention. In the nonsurgical patients the treatment was initiated as soon as the diagnosis was established; in those who had undergone surgery it was started on the 4th postoperative day. In all the cases, except one in which the patient was a child, the dose was 2 tablets a day, taken at a 6-hour interval. The child was given half a tablet twice a day, with a 6-hour interval.

In 75 (91.4%) of the 82 cases, the therapy with the novobiocin-sulfamethizole combination resulted in complete recovery, which was clinically and bacteriologically asserted within 10 to 12 days; in a few cases the treatment lasted for 28 days. The most outstanding results were obtained in a group of patients who had undergone prostatectomy. In these cases the urine became clear within 8 to 10 days, as compared with the 4 to 8 weeks usually required in such circumstances. Only 6 patients failed to respond to the treatment, and a

7th had a recurrence after a 2-week period of negative cultures. Only 4 patients suffered side-effects—2 with gastrointestinal disorders and 2 with urticaria. It is the authors' opinion that the results obtained with the novobiocin-sulfamethizole combination represent the best results they have had in the treatment of primary or secondary genitourinary infection.

Unilateral Thrombosis of Renal Veins: Cases with Violent Hematuria Treated with Nephrectomy. J. Nielsen, W. Permin and K. Schourup. Nord. med. 61:849-852 (June 4) 1959 (In Danish) [Stockholm].

Renal vein thrombosis, according to the literature, occurs equally frequently in both sexes and is equally often bilateral and unilateral. There may be massive or microscopic hematuria and not infrequently transitory hematuria. The etiology is unknown. The prognosis, which according to the literature is unfavorable, can probably be improved by anticoagulation treatment introduced early. In case of unilateral disease, nephrectomy can be considered, to hinder the development of atrophic kidney. Two cases seen at a year's interval in Bispebjerg Hospital were alike in symptoms and course. They occurred in apparently healthy women, aged 23 and 39 years, respectively, the younger patient being 5 months pregnant. There were no other thromboembolic symptoms. The disorder was unilateral, and the main symptoms were pain and hematuria so marked that, in spite of 10 transfusions, nephrectomy was done on vital indication. Histologically, thromboses were found in many of the interlobular and arciform veins; there were myriads of erythrocytes in the convoluted tubuli. The patients have since been well.

THERAPEUTICS

Response to Stretch of Hypertonic Muscle Groups in Hemiplegia. J. B. Brennan. Brit. M. J. 1:1504-1507 (June 13) 1959 [London].

A chance observation provided the stimulus for the work presented. A man with hemiplegia of one year's duration was fitted with a splint to prevent contracture of his knee, which was held in 90 degrees flexion by tonic spasm; the splint held his knee in full extension. Next seen a month later, the patient explained that he had worn the splint constantly. He had found it comfortable to wear, and it had enabled him to walk, so he had not risked its removal, fearing his spasm might return. On examination it was found that hypertonus in the hamstrings had been abolished and that voluntary extension, previously absent, could be performed against resistance. Tonus in the quadriceps, originally mild, had become appreciable, but voluntary flexion had not been much affected. The patient had had no other treatment during that month, and it seemed probable that this new distribution of tonus in the flexors and extensors of the knee was a result of stretching the former and shortening the latter constantly for a time. It was a most desirable change, since it enabled the man to walk.

Fourteen hemiplegic patients were selected, and the response to stretch of 19 flexor muscle groups —18 in the upper limbs and 1 in the lower—was studied. The average duration of hemiplegia before beginning treatment was 18 months. The results obtained support the thesis that the tonic muscle spasm shown by certain flexor muscle groups in patients with residual hemiplegia can be abolished by submitting the muscles to a long period of stretch. This was effected by keeping the appropriate joints, originally held flexed by spasm, extended in splints. Each was constantly stretched for an average period of 3 months and for diminishing daily periods during the succeeding 2 months. Control was exercised by observing any spontaneous change in the neighboring unstretched groups in each patient. Hypertonus was abolished in all the treated flexor groups. Voluntary flexion was not impaired except in one case. The antagonist muscles achieved an increased power and range of movement in most cases. No lasting spontaneous change occurred in any of the control muscle groups.

Ten patients in the series studied still survive. Of these, 6 have retained the above features in all 9 stretched muscle groups and their antagonists during an average period of 58 weeks since stretch was stopped. Six muscle groups in 4 patients have reverted to their original state in a similar time. The factors which may be responsible for this variable response are suggested.

Arteritis Caused by Hypersensitivity to Methylthiouracil. F. Hogewind, H. N. Hadders and L. Meyler. Nederl. tijdschr. geneesk. 103:1009-1012 (May 9) 1959 (In Dutch) [Amsterdam].

After citing several literature reports on the development of arteritis during or after the use of thiouracil derivatives, the authors present the case of a 33-year-old man with toxic diffuse goiter (Basedow's disease), who during 3 weeks in the hospital was given daily 200 mg. of methylthiouracil. This had the effect that the basal metabolic rate decreased from +54 to +14. After the patient's discharge treatment was continued, at first with daily doses of 100 mg. and later of 50 mg. of methylthiouracil. With this maintenance therapy the patient remained in fairly good condition, except that occasionally blood tests revealed eosinophilia.

After the methylthiouracil therapy had been continued for 2¼ years, the patient was hospitalized again, complaining of sore throat, pains in knees and elbows, chest pain on the left side, and occasional vomiting. Because of joint pains he had recently also taken a salicylate. He appeared ill, with fever and symptoms of pericarditis with effusion. He had pleurisy on the left side, and later also on the right. Several joints were painful and swollen. There was proteinuria and increased blood pressure. These symptoms gradually disappeared when the patient was given corticotropin (ACTH), with continuation of the methylthiouracil therapy. Reduction in the ACTH dosage, however, was followed by a relapse, after which the methylthiouracil medication was discontinued. After 5 weeks' treatment with prednisone and ACTH, the man was discharged. The authors believe that the inflammation of the small arteries which developed in this patient was a result of the treatment with methylthiouracil. Signs of polyserositis often accompany this condition.

Side-Effects of Tetracycline Alone and of Tetracycline with Nystatin. R. Larkin. Lancet 1:1228-1229 (June 13) 1959 [London].

Tetracycline probably remains the most dependable drug for the treatment of the acute "flare-up" of chronic, nonspecific respiratory infections; but distressing side-effects are fairly common. Childs, in 1956, found that nystatin inhibited the increased growth of Candida albicans observed in the feces of patients treated with tetracycline, but there is disagreement about the ability of nystatin to modify the incidence of gastrointestinal and other side-effects caused by tetracycline. In the study presented, a total of 98 adult patients, mainly with acute or chronic respiratory infections, were placed at random in 2 groups. Those in one group (55 patients) were treated with 250 mg. of tetracycline hydrochloride 4 times daily, and those in the other group (43 patients) with 250 mg. of tetracycline hydrochloride and 250,000 units of nystatin 4 times daily. Clinical side-effects were recorded in terms of gastrointestinal discomfort, diarrhea, and anogenital pruritus. In the latter part of the trial rectal and throat swabs were taken on the 5th day of treatment and examined for the presence of C. albicans and other yeasts.

Gastrointestinal disturbances were noted in 37 of the 55 patients on tetracycline alone, and in 4 of the 43 on tetracycline plus nystatin. Diarrhea developed in 9 of the former group but in none of the latter group. On the 5th day of treatment rectal swabs positive for yeasts were obtained from 11 out of 19 tetracycline-treated patients and from 2 out of 18 given the tetracycline-nystatin combination. Oral thrush developed in 3 of the 19 patients given tetracycline alone but in none of the 18 who received nystatin in addition. Since nystatin is antifungal and has little effect on bacteria, viruses, and various animal cells, it seems reasonable to assume that suppression of fungi is responsible for the reduction in side-effects. This assumption is supported by the frequent isolation of C. albicans and other yeasts from rectal and throat swabs taken from patients who complained of gastrointestinal disturbances. The simultaneous administration of nystatin with tetracycline inhibits the overgrowth of fungi in the intestines and has a similar, although less pronounced, effect on yeasts in the throat. In addition to affording protection against the direct invasion of tissue by C. albicans leading to clinical moniliasis, nystatin apparently can reduce gastrointestinal disturbances substantially during the oral use of tetracycline hydrochloride, which disturbances may be fungal hypersensitivity reactions.

Oral Tartar Emetic Treatment of Schistosomiasis Japonica. Y. C. Mao, S. C. Sheng, C. K. Tu and others. Chinese M. J. 78:532-541 (June) 1959 (In English) [Peking].

The clinical results obtained with the oral administration of a tartar emetic compound to 556 patients with schistosomiasis are reported. These patients, selected from more than 3,000 treated by the authors, were at different stages of chronic schistosomiasis; all had positive findings of cercariae in the stools. There were 512 males and 44 females in the series; the ages ranged from 5 to 66 years, with the great majority in the young adult category. Most of the patients (485) were treated at 2 hospitals and a clinic in Chinua; 20 were treated at home or at their place of work; and 51 were treated at the Chinua Agricultural School without interruption of attendance.

The tartar emetic compound used for treatment contained equal parts of tartar emetic and sodium bitartrate in enteric-coated capsules or tablets of 10 and 50 mg. For adults the initial dose was 30 mg. taken in 3 tablets or capsules a day. The dose was increased to 60 mg. on the second day, to 150 mg. on the third, and to 300-450 mg. from the fourth day on, until the patient had received a total dosage of 100 to 120 mg. per kilogram of body weight. The shortest duration of the treatment was 10 days, in children; the longest was 22 days; in most cases it was 17 days. The therapeutic effects were evaluated by the results of stool examination and the improvement in the clinical condition. Of 357 patients for whom stool examination was performed, 285 had negative findings at the end of the treatment. The clinical improvement consisted mainly in reduction in size of the liver and spleen, decrease or disappearance of ascites, disappearance of dysentery symptoms, and increase in working capacity and appetite, with a general feeling of well-being.

The immediate over-all effect of the tartar emetic treatment was evaluated in 90%, and the remote effect in 60%, of the patients. The untoward reactions observed were mainly gastrointestinal disorders, which disappeared rapidly with interruption of the therapy or a reduction in the dosage. In 98% of the cases the patients tolerated the reactions and were able to complete the treatment. The number and severity of the reactions decreased when a satisfactory coating was obtained for both the capsules and the tablets. The authors point out the advantageous features of the oral administration of a tartar emetic compound; it is a comparatively safe, simple, and inexpensive method of treating schistosomiasis, which can be carried out at the patient's home or place of work.

Research on the Diuretic and Salt Diuresis Promoting Activity of Hydrochlorothiazide: Preliminary Clinical Study. G. Casirola and D. Meduri. Minerva med. 50:1608-1613 (May 26) 1959 (In Italian) [Turin, Italy].

The authors report on the effect of hydrochlorothiazide on 45 patients, 30 to 82 years of age, who suffered from disturbances of water and salt metabolism. Eleven patients presented hepatic cirrhosis, with ascites; 25, cardiac insufficiency, with edema; 4, edematous nephrosis; and 5, neoplasms, with edema or ascites. Hydrochlorothiazide was given to each patient in the morning and again after 12 hours. Three patients with cirrhosis received 50 mg. of the drug per day for 19 days, 4 received 75 mg. per day, 3 received 100 mg. per day, and 1 received more than 150 mg. per day. An increase in the daily volume of urine, in some cases of more than 3,000 cc. per day, was observed in 9 of these patients. The drug had no effect on 2 patients, but these patients also had derived no benefit from chlorothiazide. With the exception of 2 patients who had taken a daily dose of 100 mg. and who suffered from diarrhea on the third and fourth days of treatment, the drug was well tolerated. Best results were obtained in patients who received a daily dose of from 50 to 75 mg. per day. Ascites was checked within 40 days in 4 patients.

A 75-mg.-per-day dose was the optimal daily dose for promoting salt diuresis; it gave results far superior to those obtained with a dose of 1,500 mg. of chlorothiazide per day. Good results were obtained also in the cardiac patients; 5 of these patients, however, did not respond to treatment with either hydrochlorothiazide or chlorothiazide. The optimal doses among the other 2 groups ranged from 25 to 75 mg. per day. Satisfactory results were obtained in the symptomatic treatment of edema in patients with neoplasms. The results in patients with nephrosis were proportional to the extent of involvement of the parenchyma of the kidney.

The authors point out that hydrochlorothiazide is absorbed rapidly from the intestine, is nontoxic, causes no side-effects, favors the elective elimination of the sodium ion and the chloride ion, and has no effect on the elimination of potassium. It has its best effect with a dose 30 times smaller than the dose needed with other diuretics. It can be given to patients who are being treated with substances that increase the elimination of potassium, and has a hypotensive effect in patients with hypertension.

RADIOLOGY

Suprasternal Thoracic Aortography: Suprasternal Transthoracic Needle Puncture Opacification of the Thoracic Aorta. J. S. Lehman, W. M. Lemmon, R. A. Boyer and E. A. Fitch. Radiology 73:18-36 (July) 1959 [Syracuse, N. Y.].

The authors report on 92 patients, between the ages of 14 and 60 years, and a 3-year-old child, in whom 110 attempts at opacification of the thoracic aorta were made by a transthoracic needle puncture in which a suprasternal approach was used. A 17-gauge, thin-wall needle of 7-in. length was employed. The needle was connected by a 14-in. length of special high-burst strength, but reasonably flexible, plastic tubing to a special large-bore 3-way stopcock. From the stopcock the system was connected by a 40-in. length of plastic tubing to a pressure injection apparatus and also to a capacitance-type electromanometer and direct writing polyoscillograph. Pressure tracing and electrocardiographic monitoring were recorded simultaneously. Diatrizoate sodium in either 85 or 90% concentrations was used as contrast medium. The radiopaque medium was injected in 84 of the 110 attempted examinations, 68 of which were performed for demonstration of the presence and/or degree of aortic valvular insufficiency, 38 for the primary purpose of determining the status of the coronary arterial system, and the remaining 4 for evaluation of suspected patent ductus arteriosus. Of the 84 examinations in which injection was made, aortic opacification resulted in 78; of the latter, satisfactory needle penetration was accomplished with one needle pass in 46, 2 needle passes in 14, 3 passes in 9, 4 passes in 8, and 5 passes in 1. Important complications, including moderate to severe shock, occurred in 7 patients.

The ultimate place and value of this procedure of suprasternal thoracic aortography are yet to be determined. The procedure is to be considered another method of direct delivery of a radiopaque medium to the ascending aorta and, as such, can effect excellent opacification of the thoracic aorta and its branches. The direct demonstration of regurgitant reflux from the aorta into the left ventricle can be achieved, and such demonstration under the conditions of the procedure, as employed by the authors, is, as they interpret it, evidence of dynamic aortic valvular insufficiency. Some estimation or quantitation of aortic insufficiency is also possible by the procedure. By its application to coronary artery opacification, rather satisfactory demonstration of the coronary system can, on occasion, be obtained. The procedure is not without real hazard. The potential dangers of needle trauma—tear of the aortic wall or other mediastinal vascular structures, intramediastinal or intrapericardial hemorrhage, laceration of a coronary artery or aortic valve cusp, aortic intramural or para-aortic injection of radiopaque medium, and pneumothorax—must be considered. Considering the small size of the aorta in infants and children, it appears at present that the procedure presents too much risk, and its accomplishment is too difficult, to adapt it to such patients.

Emphasis should be placed on the following factors to obviate possible complications: (1) careful study of preliminary chest roentgenograms to determine as accurately as possible the direction of needle insertion and the maximal permissible distance of the needle advancement; (2) scrupulous attention to the pressure wave recordings, and withholding of the radiopaque injection if there is any suggestion of pressure wave "damping"; (3) avoidance of any voluntary or involuntary movement of the patient, especially the head and neck, during or after intramediastinal insertion of the needle; (4) strict attention to the prevention of any further movement of the needle other than that transmitted by the aortic pulsations, once the needle has been satisfactorily positioned; (5) conservatism regarding repeated needle passes; no more than 4 needle passes should be permitted to obtain satisfactory intra-aortic positioning of the needle; and (6) discontinuance of the procedure at the earliest sign of any aberration in patient reaction, persistent electrocardiographic changes, or technical difficulties.

Percutaneous Implantation of Radiogold into the Hypophysis in Patients with Metastasizing Mammary or Prostatic Carcinoma. E. Frey and U. Cocchi. Schweiz. med. Wchnschr. 89:652-656 (June 20) 1959 (In German) [Basel, Switzerland].

The severe pains caused by skeletal metastases in patients with mammary or prostatic cancer present a difficult therapeutic problem, because patients may become addicted to analgesics. Since there have been reports that these pains respond to hypophysial implantation with radioisotopes, the authors used Bauer's radiogold (Au^{198}) method. Puncture of the sella turcica is done by the percutaneous, paranasal, transethmoidal, transsphenoidal route. The technique is comparatively simple and is tolerated even by patients in a very reduced condition. The hollow needle employed has a pointed mandrin for advancing it, and 3 blunt mandrins of different lengths for the introduction of the radiogold seeds, each of which contains 10 mc. of Au^{198}. Except for one woman, with an especially small sella turcica, in whom 3 seeds (30 mc.) were implanted, 4 radiogold seeds were implanted in the 8 patients of the series. These included 7 women with metastatic mammary carcinoma and 1 man with metastatic carcinoma of the prostate. No deaths resulted from the treatment, and all the patients experienced pain reduction, 2 being practically freed from pain. Whereas the progression of the osseous metastases was arrested, the metastases in the liver and lung seemed not to be influenced. Clinical and histological observations indicated that it is impossible to destroy the entire hypophysis by central implantation of 4 radiogold seeds.

Value of Radiologic Signs in the Malabsorption Syndrome: Changes Following Treatment. I. Larrechea, M. M. Mejilla, A. Schapira and V. d'Alotto. Prensa méd. argent. 46:178-185 (Jan. 16) 1959 (In Spanish) [Buenos Aires].

One of the most important problems in the radiologic diagnosis of sprue is the interpretation of the variety of signs which are mere manifestations of functional disorders. The authors studied the diagnostic and the prognostic value of radiologic findings in 11 cases of primary malabsorption syndrome and compared the radiograms taken before and after treatment and during periods of remission. There were 5 males and 6 females in the series, with ages ranging from 10 to 53 years. All the patients had been given a diagnosis of malabsorption syndrome, established by clinical and laboratory findings. Each patient had had radiograms of the small intestines taken in ventral decubitus every hour during a 5-hour period. The pictures showed dilatation of the intestinal folds in 6 patients, segmentation in 9, hypersecretion in 11, thickening of the plicae in 10, moulage in 6, and alterations in motility in 6. Comparing the clinical and radiologic pictures of each patient, it was found that the characteristic most closely related to seriousness of the disease was dilatation. It was also found that in the 6 cases in which dilatation of the intestinal folds was present it was associated with other intestinal abnormalities.

In 9 patients treated with prednisone, folic acid, and vitamins, it was possible to take post-therapy radiograms and observe if there had been any changes in the intestinal picture. Only one patient, who had been discharged after complete clinical recovery, had a normal radiogram. The authors conclude: 1. The presence of radiologic signs of dilatation of the intestinal folds indicates a severe form of the malabsorption syndrome. 2. The association of this dilatation with other radiologic signs of intestinal abnormality constitutes a criterion for diagnosis of the disease.

BOOK REVIEWS

Antibiotics: Their Chemistry and Non-Medical Uses. Edited by Herbert S. Goldberg, Ph.D. Contributors: Herbert S. Goldberg and others. Cloth. $15. Pp. 608, with illustrations. D. Van Nostrand Company, Inc., 120 Alexander St., Princeton, N. J.; 257 Fourth Ave., New York 10; D. Van Nostrand Company, Ltd., 358 Kensington High St., London, W. 14, England; 25 Hollinger Rd., Toronto 16, Canada, 1959.

The title of this book might be misleading to those not having had an opportunity to review it. Actually, anyone interested in antibiotics, whether their field is medical or nonmedical, should find it an excellent reference source. The first two chapters cover basic material on antibiotics, including antibacterial effects, mode of action, and chemistry. The next four chapters cover the use of these drugs in nutrition, in plant disease control, food preservation, and their use in the isolation of pure cultures. The final chapter discusses in detail the public health significance of the nonmedical uses of antibiotics. The organization of the book is good, and the clinician readily will note from the last chapter that the nonmedical uses of antibiotics really become medical problems, since such uses may result in antibiotic residues in foods, including meats, milk, fruits, and vegetables, that are consumed by man. Ingestion of antibiotic residues may cause allergic reactions, superinfection, or the development of resistant micro-organisms. The book contains several thousand references, most of them abstracted in the text. It is well written, makes good reading, and should be of great value as a reference volume for the interested clinician.

The Truth About Your Eyes. By Derrick Vail, M.D. Second edition. Cloth. $3.50. Pp. 180, with 6 illustrations. Farrar, Straus & Cudahy, Inc., 101 Fifth Ave. New York 3, 1959.

Written for the layman, this revised edition presents in simple, concise language the most interesting and important information about eyes desired by patients. Among the abnormalities discussed are cataract, glaucoma, muscular anomalies, refractive errors, injuries, and infections. The fundamentals of ocular development, anatomy, physiology, and hygiene are briefly presented. The objective discussion of current controversial subjects such as contact lenses, cycloplegics, ocular exercises, eye glasses, eye strain, and vitamins is especially good. This book can be read with profit by ophthalmologists and other physicians because it facilitates clear, authoritative answers to many patients' inquiries and is an aid in preparing educational talks to laymen. Intelligent laymen who have read this book agree that it is interesting and informative. One suggested that several of the more technical discussions, including that on cranial nerves, should be condensed.

In the next edition, greater emphasis should be placed on the aggravating effect of emotional excesses and nervous tension on numerous functional and structural eye diseases including many glaucomas, allergic manifestations, and vascular retinopathies. The popular misconception that all of every patient's ocular symptoms are due to a single and all-inclusive cause and that its removal will promptly result in complete recovery should, if possible, also be corrected. Following the present trend that mass education is an important step in the prevention and treatment of disease, the author's broad experience has made possible this practical contribution which is of interest especially to eye patients and ophthalmologists.

Recreation in Total Rehabilitation. By Josephine L. Rathbone, Ph.D., Associate Professor, Department of Health Education, Physical Education and Recreation, Teachers College, Columbia University, New York, and Carol Lucas, Ed.D. Cloth. $9.50. Pp. 398. Charles C Thomas, Publisher, 301-327 E. Lawrence Ave., Springfield, Ill.; Blackwell Scientific Publications, Ltd., 24-25 Broad St., Oxford, England; Ryerson Press, 299 Queen St., W., Toronto 2B, Canada, 1959.

The authors of this volume feel that whether recreation is considered a type of therapy or wholesome activity is beside the point as long as it contributes to the welfare and recovery of the patient. The general mission of the book is to explore the recreational experiences that can be helpful to a patient and the kind of skills needed by the recreation leader who provides them. Rehabilitation today is a team affair in which the team may range from only a physician and a member of the patient's family, to a physician, nurse, therapists, and others. Whatever the size and kind of the team, the physician is captain or quarterback. He calls the plays and directs the team—"evaluates the patient, prescribes activities, and coordinates and integrates the various parts of the program, as it applies to each patient."

The physician evaluates and prescribes for the patient on three bases—physiological, kinesiological, and psychological—and each member of the rehabilitation team, including the recreation leader, must understand the patient's assets and liabilities in these areas. Otherwise he may do physiological, kinesiological, or psychological harm to the patient in carrying out the prescription. This requires that

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These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

the leader have appropriate medical orientation as well as proper recreational preparation for his role. The exact nature of the necessary medical orientation has not been defined, but there is general agreement that it should be at the graduate level and in a school affiliated with a medical college or at least a teaching hospital.

The book goes on to outline problems found in institutions serving the ill and handicapped and to describe some of the medical indications for recreational activities and how such experiences may help the patient. The rest of the volume is devoted to recreational activities and their adaptation and programing for the ill and handicapped. This goes far beyond games and sports to include music, the graphic and plastic arts, crafts, hobbies with special emphasis on collections and nature lore, literature and the theatre, writing and acting, dancing, and special events. This volume should have its greatest value as a guide for recreation leaders preparing themselves in rehabilitation and undergoing orientation in the medical setting. Such persons should find much of the text familiar in terms of recreation principles and practices but also much that is new and helpful in their suggested application for the ill and handicapped. To some extent the opposite is true; those on the rehabilitation team whose orientation is therapeutic may here find a new interpretation of recreation.

Diabetic Manual for the Patient. By Elliott P. Joslin, M.D., Sc.D. Tenth edition. Cloth. $3.75. Pp. 304, with 41 illustrations. Lea & Febiger, Washington Sq., Philadelphia 6, 1959.

Now in its 10th edition, this is the oldest and best known of the many popular manuals for the guidance of diabetic patients and their families. The first edition appeared in 1918, so this manual has been frequently and continuously revised for more than 40 years. Its author has observed and treated diabetic patients for more than 60 years. As with all other forms of teaching by this well-known group of physicians, the underlying theme of the manual is firm insistence on prevention of abnormal hyperglycemia and glycosuria by means of quantitative diet, insulin (or in certain cases orally given hypoglycemic compounds), and exercise. The author favors insulin over orally given agents and restricts the use of the latter to tolbutamide, but approves of the use of several other orally given compounds by members of the staff. The prevention and management of common complications are stressed, and various psychological, habitual, and even economic attitudes are recommended.

The style of the book is simple and direct. Its author's gentle, inspiring, interested, and interesting personality are mirrored in every page and illustration.· Answers to almost every question any diabetic could ask are given in detail, even to the extent of some repetition. Because of the experience, wisdom, and missionary spirit reflected by this manual it can be recommended for all diabetic patients and families, old and new, above all others in the field.

Conquering Your Allergy. By Boen Swinny, M.D. Cloth. $3.95. Pp. 221. Fleet Publishing Corp., 70 E. 45th St., New York 17, 1959.

While this book for the layman has some factual material of value to the allergic person, this basic information is lost in a maze of unorthodox beliefs, inaccuracies, unnecessarily lengthy anecdotes, and recurring boasts. Among the misconceptions are the inclusion among allergic manifestations of Horton's syndrome, Ménière's disease, and "emotional reaction to rainy days, rock n' roll music, or a visit from your mother-in-law," while making no mention of the allergic aspects of blood diseases (thrombocytopenia and acquired hemolytic anemia) or other possibilities of autosensitization. One must disagree with the author's belief that allergic shock from an injection of almost any medication can be forecast by a prior skin test, that no one but a dermatologist or roentgenologist should use x-rays, that the case fatality rate from anaphylactic shock caused by penicillin is as high as he implies (from his statement one can compute that there would be about 500,000 such deaths in the United States), that lay people should be furnished with a complete list of drugs and details of their use, that an author should discuss fees, or that the size and efficiency of his professional staff should be extolled. Since there are several more informative and more accurate books on allergy available to the public, there appears to be no need for this particular book.

Synopsis of Ophthalmology. By William H. Havener, B.A., M.D., M.S. (Ophth.), Professor and Chairman, Department of Ophthalmology, Ohio State University, Columbus. Cloth. $6.75. Pp. 288, with 189 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton, 134 Great Portland St., London, W. 1, England, 1959.

As more knowledge is gained in the various medical and surgical specialties, it becomes more difficult for anyone not engaged in any particular specialty to keep abreast of the advances in the latter. Any effort to spread knowledge in terms which will be useful, particularly to the general practitioner, is worthwhile. Such is the attempt made by the author of this volume. Much valuable information is contained in this small book, and many but not all of the illustrations are good and informative. The author has expanded the book to something more than a synopsis, however, by going into great detail on some subjects. Thus it is something more than a condensed statement and something less than a textbook. This diminishes its value as a ready reference to a nonophthalmologist who might be trying to track down the meaning of a particular sign or symptom.

QUESTIONS AND ANSWERS

SEQUELAE OF HYPERTENSION

To the Editor:—*Is there general agreement that a person with benign arterial hypertension is more likely to suffer a heart attack or stroke than a person with normal blood pressure? Is there a reliable statistical study which shows that the risk of heart attacks and strokes in hypertensive persons is reduced by treatment of hypertension with drugs or by any other method? What is accomplished in the treatment of benign arterial hypertension other than a reduction in the arterial pressure as measured by the sphygmomanometer? I have never been able to correlate very well the alleged symptoms of hypertension—headache, dizziness, weakness, and palpitation—with the height of the blood pressure.*

J. H. Rogers, M.D., Gadsden, Ala.

Answer.—There does not appear to be any proof that the risk of heart attacks and strokes in hypertensive persons is reduced by the treatment of hypertension. Such evidence would be entirely negative in character because we are dealing with a group in which a high incidence of vascular accidents is well documented. It is well established that the incidence of sclerosis of the small and medium sized vessels is increased over a normotensive group, and it seems logical to assume that we might be preventing such damage by reducing blood pressures. This is what one would expect from the treatment of benign hypertension.

Little can be expected from the treatment of the extremely mild or intermittent hypertensive disease. Persons who consistently have a diastolic pressure of 100 mg. Hg or above are in danger of having premature vascular accidents. It is very difficult to correlate the symptoms of hypertension with headache, dizziness, weakness, and palpitation. The most prominent symptom seems to be extreme fatigue.

CASTOR OIL AND SKIN CANCER

To the Editor:—*Has any research been done concerning the effect of castor oil or its main component, ricinoleic acid, on squamous cell cancer?*

M.D., Georgia.

Answer.—There apparently has been no investigation of the effects of castor oil or similar drugs on carcinoma of the skin. The irritative property of castor oil, when locally applied to the skin, is a known characteristic of this drug. It is necessary to point out the possible fallacy in the assumption that, because the cancer disappeared after a topical application, this effect can be attributed to the drug. The oncology of cutaneous cancer would further indicate that this could be an erroneous assumption. There is a so-called morphea type of basal carcinoma, a sclerosing form of cancer, which seemingly resolves centrally, only to advance actively peripherally, thus giving the appearance of being healed. There have also been a number of reported instances in which the spontaneous involution of epithelial carcinoma occurred within a short interval of time.

BENZENE HYDROCHLORIDE AND APLASTIC ANEMIA

To the Editor:—*A 16-year-old boy, previously in good health, has been found during the past three months to have aplastic anemia. Careful questioning about contact with possible bone marrow depressants reveals that his mother occasionally sprays chlordane about the house and that about two years ago 700 to 800 gal. of a solution containing benzene hexachloride was put into the soil beneath the concrete blocks on which the house is built. A definite odor of insecticide still emanates from the bathroom floor about the pipes. The concrete slab does not cover these pipes in accordance with FHA requirements. Could the benzene hexachloride in the soil be responsible for this boy's aplastic anemia? How can one determine if it is safe for others to occupy this house? Please suggest a way to eliminate possible dangers.*

Henry M. Gewin, M.D., Mobile, Ala.

Answer.—A dogmatic answer to the question cannot be made at present. Exposure to benzene hexachloride used in vaporizers has been reported to cause angioneurotic edema, skin sensitivity, urticaria, irritation to the eyes and upper respiratory tract, and anemia (report to the Council on Pharmacy and Chemistry, *J. A. M. A.* 152:1232-1234 [July 25] 1953). In many instances, a direct causal relationship has not been established. In that report, cognizance was taken of the claim that benzene hexachloride may cause depression of the bone marrow, but the evidence was not regarded as conclusive. More recently, a critical review of the causes of acquired aplastic anemia cited three patients who developed the disease after exposure; there

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The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

was additional contact with chlordane, benzene, and/or chlorophenothane (DDT) in each instance (Scott and others, *Medicine* 38:119, 1959).

About all one can say with certainty, therefore, is that benzene hexachloride (and chlordane) may possibly be responsible for a rare case of aplastic anemia. Even if this be true, there probably is marked variability in the susceptibility of different persons to the toxic effect. Since no method of detecting susceptibility currently exists, the safest procedure would be to seal the openings around the pipes. The engineering problems involved in such a seal are unknown to this consultant. Under the existing conditions, the concentration of benzene hexachloride must be much smaller than when the material is distributed from a vaporizer. To what extent the repetition of exposure would compare to the lesser concentration is, of course, another unknown.

SEROLOGIC EVALUATION

To the Editor:—*A patient recently had a Wassermann test with results reported as weakly positive. He had had primary syphilis 30 years earlier and was treated with arsphenamine (and probably mercurials), after which he was informed his blood test result was negative. He later married and had one child, a daughter who has had no signs of the disease. His physical examination indicates no evidence of complications. Does he require treatment now or in the future? What form of treatment would be indicated?*

Edwin P. Bickler, M.D., Milwaukee.

Answer.—Serologic tests performed 30 years ago were not as sensitive as they are today. A weakly positive serologic reaction which is unaccompanied by signs or symptoms of syphilis is not uncommon, and therefore no treatment is indicated. Serologic tests and physical examination should be made at proper intervals. A reactivation of the disease in this patient is not likely.

VITAMINS AND DANDRUFF

To the Editor:—*One of my patients has been told by a non-M.D. skin specialist to take vitamins for his dandruff. I do not wish to be unfair to my patients nor to have them continue taking something which, to my knowledge, will not help. Please comment.*

Martin Karr, M.D., San Mateo, Calif.

Answer.—There is no vitamin used topically or systemically which dependably clears dandruff. A number of scaly and seborrhea-like syndromes in laboratory animals have been described after induced deficiencies of various vitamin and nutritional factors, but such changes have not been consistently reproduced in humans. Riboflavin deficiency may produce certain seborrheic eczema-like changes, seen often at the nasolabial folds. In an American such skin changes rarely respond to the administration of riboflavin alone. The topical use of pyridoxine is reported to be helpful for seborrhea and seborrheic eczema, but this consultant was not able to corroborate these reports. Money spent on vitamins to clear dandruff would be better spent on good food and one of the several modern shampoo remedies for dandruff.

CARPAL TUNNEL SYNDROME

To the Editor:—*What is the relationship of the carpal tunnel syndrome to systemic diseases? What are the diseases involved? Is there any reported association of collagen diseases with this syndrome in the pediatric age group?*

Milton Jabush, M.D., Lakewood, N. J.

Answer.—References to carpal tunnel syndrome are not common in orthopedic literature. They usually deal with the motor and sensory dysfunction associated with compression of the median nerve, which prevails in adults, and children are not mentioned. In more than 60 cases the following points are of interest in relation to these questions: The youngest patient was 29 years of age; the etiology was related to trauma (injury or occupational) or was classified as idiopathic; and in no instance was there any suggestion of a prevailing systemic disease.

Diseases in which there is an excess deposition of collagen are stated by Everett (Medical Biochemistry, ed. 2, New York, Paul B. Hoeber, Inc., 1946, p. 411). The carpal tunnel syndrome is not known to prevail as a complaint in any of these disorders, including those which are most frequently associated with childhood.

PATCH TEST FOR POISON IVY

To the Editor:—*When a suspected sensitive patient was patch tested for poison ivy, three disks of strengths 1:100, 1:1,000, and 1:10,000 were used; the strongest and weakest patch areas showed no reaction, but the other showed a strongly positive reaction (3+ erythema, edema, and a few vesicles). An allergist named this as the prozone phenomenon. If this is true, please furnish a reference which will describe this phenomenon. If false, what is the name given to this reaction?*

R. J. Sexton, M.D., Charleston, W. Va.

Answer.—The prozone phenomenon occurs only in the laboratory and never in vivo. It is seen in precipitation tests and at times in agglutination or complement-fixation tests. It is due to the presence of an excess of antibody. The term "prozone" is becoming obsolete and is being replaced by "zone of antibody excess." The occurrence of the positive patch tests with the 1:1,000 dilution and not with 1:100 could not be an evidence of a prozone phenomenon. There must have been an error either in technique or in preparation of the disks. It is suggested the test be repeated with the same disks or, preferably, with three different disks of definite known strength. This consultant knows of no reference describing the reaction mentioned. A description of the prozone phenomenon can be found in most immunology books.

STEROID TREATMENT OF ALOPECIA

To the Editor:—*Would methylprednisolone be of value in treatment of alopecia resembling alopecia areata but of traumatic origin? The patient is a 39-year-old man, who seven years ago received second-degree burns on the temporal regions of the head from cosmetics used in a hair treatment. When the scalp healed the burned areas remained completely bald until two years ago. Within the past two years slight hair growth has occurred, spontaneously, but not in sufficient quantity or quality to achieve a good cosmetic appearance. The patient is in good health. The recent conference on hair growth and regeneration held in New York reported that methylprednisolone in treatment of alopecia areata would be of value only if used within five years of the onset of the condition.*

Gerald C. Haskell, M.D., Springfield, Ohio.

Answer.—It is necessary to decide whether the patient has alopecia areata or cicatrizing alopecia secondary to the burns. If the gross clinical features are not distinctive, a biopsy might give the information. If the hair follicles are not completely destroyed, the prognosis is more hopeful. Should this be true alopecia areata without associated cicatrizing alopecia, regrowth of hair is possible, even at this late date. The use of orally given steroids has been followed by hair regrowth in some instances, but hair fall, it is said, recurs when the treatment is discontinued. Such therapy should be reserved for severe types of alopecia areata, totalis, or universalis with realization that steroid therapy may be necessary for a prolonged period of time. Local injection or tattooing of steroids into patches of alopecia areata has given good results in some cases, though superficial atrophy has been observed after such treatment. In this case, since some spontaneous regrowth has begun, it may be best to observe the patient frequently and perhaps use standard stimulating measures such as ultraviolet-ray therapy, painting with mild phenolic solutions, and light dry-ice treatment. In all cases of alopecia areata the prognosis should be guarded but not hopeless.

ISOLATION CARE WITH INFECTIOUS HEPATITIS

To the Editor:—*What is the current recommendation for isolation techniques used in cases of infectious hepatitis? What routine should be used in hepatitis cases after necessary surgical or obstetric procedures have been done? What techniques should be followed in the operating room when unsuspected hepatitis is found during surgery?*

William F. Cox III, M.D., Baltimore.

Answer.—Infectious hepatitis caused by virus A probably is disseminated in fecal material. Rigid hygienic techniques for the handling of infected patients and their feces minimizes the risk of contamination. The patient is regarded as being infectious for about three weeks. If the condition becomes chronic the interval may be longer. In some areas the disease, which may reach epidemic proportions, is most prevalent during the winter and autumn months, so droplet infection has been considered. Water, milk, and other foods, improperly handled, may act as vehicles, especially if the handler be a carrier for hepatitis. The blood stream of a person infected with either virus A or virus B of serum hepatitis carries live virus. Autoclave terminal sterilization of all linens and instruments must be done after operation in patients with known cases and cases discovered during operation. Instruments which will not withstand sterilization by heat should be destroyed by incineration.

STAINING OF TEETH

To the Editor:—*A layman has been told by a prominent pediatrician and a dentist that multiple-vitamin preparations could cause staining of teeth in young children. The dentist advised use of preparations containing vitamins A, D, and C only instead of those containing the vitamin B complex. The child has teeth that look iron-stained, though she has never taken iron preparations. Please give an opinion.*

Beatrice Hawkins, M.D., Brownsville, Texas.

Answer.—Apparently there are no published reports that associate multiple-vitamin preparations with staining of teeth. The materials usually present in vitamin B–complex preparations for pediatric use would not act as chemical stains for the tooth surfaces. It is extremely difficult to stain dental enamel, even with histological dyes. Intrinsic green staining of enamel has been reported in association with a history of neonatal jaundice. The question notes the relationship between iron compounds and dental stain. There is also a possibility that the observed condition may be due to the action of chromogenic bacteria. Such factors may bear further investigation in this patient.

WASHINGTON NEWS

Crackdown Urged on Amphetamine Sales . .
Medical-Health Appropriations Boosted . .
A. M. A. Stand on Disability Program . .
Warning on Cranberries . .
Dentifrice Advertising . .

ILLICIT AMPHETAMINE TRAFFIC

HEW Secretary Arthur S. Flemming said the administration may recommend legislation next year to crack down on the illegal sales of amphetamine drugs. He told a news conference that a campaign by the Food and Drug Administration against bootlegging such drugs "has disclosed a serious breakdown in our system of marketing controls for these drugs."

Justice Department agents have found more than 800,000 amphetamine tablets in the hands of wholesale peddlers, Flemming pointed out. FDA officials believe that the roundup of violators so far has only scratched the surface of the total illicit traffic in such drugs, he said.

Evidence has been obtained that more than 200 operators of truck stops and similar establishments were selling amphetamine tablets, according to Flemming.

"In view of the magnitude of the traffic in these drugs, I believe the present law does not provide the most effective way to get at the problem," said the secretary. "We are therefore considering ways in which the legislative authority for dealing with this situation can be improved, and I expect that we will have a constructive proposal in this area to submit to the next session of Congress."

Under serious consideration, he said, are four proposals. They would require manufacturers, wholesalers, and retailers to be registered so that they could be subject to federal inspection; require records of sales of the drug with penalties for falsification; provide that unauthorized possession of the drug is an offense; and provide that any illegal sale of the drug is a federal offense, even though it involves intrastate shipments, on grounds that sale of the drug is a "burden" on interstate commerce.

MEDICAL-HEALTH APPROPRIATIONS BOOSTED

Congress voted 216 million dollars more for federal medical-health activities for the current fiscal year than was appropriated last fiscal year. All told, such programs accounted for 3.2 billion of the about 781-billion-dollar budget. The National Institutes of Health (NIH) led the list of agencies receiving increased funds, with 104 million more this fiscal year than last, for a total appropriation of 400 million dollars.

Not listed as part of appropriations but included in the report was the estimated 5.1 billion dollars expected to be paid to disabled persons this fiscal year through programs financed entirely or in part by the federal government. This is an increase of $372,800,000 over last fiscal year which ended June 30. Such programs are financed through trust funds, not appropriations, and are supposed to be self-supporting.

The Department of Health, Education and Welfare, of which the NIH is a part, had a medical-health budget of 1.3 billion dollars for the current fiscal year, some 180 million dollars more than last year. This was the highest single budget in the field for any agency.

Next came the Veterans Administration, with appropriations of $939,700,000, an increase of about 40 million dollars over last year. The Defense Department received $753,100,000 for its medical activities, about 2 million dollars more than last year. These three agencies handle the bulk of the federal government's work in this field.

Other medical appropriations were to the Atomic Energy Commission, $52,100,000; International Cooperation Administration, $45,700,000; Department of State, $23,700,000; National Science Foundation, $27,400,000; and federal employees' health programs, $11,500,000.

A. M. A. STAND ON DISABILITY PROGRAM

A spokesman for the American Medical Association told Congress the social security disability program should continue to be a federal-state responsibility rather than a completely federal plan, as some have recommended.

Dr. Charles Farrell, Pawtucket, R. I., testifying before a House ways and means subcommittee, declared that "from years of experience with various governmental programs, the medical profession has reached the conclusion that it can make its most effective contribution where such programs are administered on a decentralized basis."

Representatives of labor unions in other testimony had advocated shifting the program to a strictly federal basis, on the grounds that this would be more efficient. However, Dr. Farrell said, "differences in local customs and conditions require negotiations and arrangements on a state-by-state basis. This method of administration results in a more ready exchange of ideas, better communication, cooperation, and understanding.

"The accessibility and ease of communication which exists under the social security disability program has facilitated the recognition and resolution of problems which might otherwise be neglected or remain unrecognized in the welter of administrative detail and procedure. We urge the continuation of this principle as an aid to the public and to the Congress in assuring the fulfillment of the intent of this legislation."

Officials of the Social Security Administration also opposed having the federal government take over the entire program.

Dr. Farrell also proposed that, when additional medical data are needed for sound determination of a disability case, "the information should be obtained from the claimant's own physician, if possible, in a manner similar to the way it is now obtained from a 'consulting physician.'

"The Bureau of Old Age and Survivors' Insurance should be authorized to require the state agency to make arrangements with the medical profession in the respective states that will permit them to purchase these supplementary examinations, laboratory [tests,] or other tests from such physicians and under such circumstances as to promote further doctor-patient relationships and rapid development of comprehensive information," he said.

There are cases in which the patient's own physician fills out forms on the basis of past knowledge of the patient and in which another examination is required. This is done by a consultant, who is reimbursed, Dr. Farrell noted, with no payment to the patient's own physician for the work he has done.

The subcommittee, headed by Rep. Burr P. Harrison (D., Va.), is studying the administration of the program and ways in which it could be improved.

WARNING ON CRANBERRIES

Arthur S. Flemming, secretary of Health, Education and Welfare, said a chemical known to cause cancer in animals has contaminated some cranberries grown in Oregon and Washington, which produce about 10% of the nation's crop. He urged that cranberries from the northwest be taken off the market until the extent of the contamination is known.

The warning came after Food and Drug Administration officers reported some cranberry shipments from the northwest contained aminotriazole, a weed killer used in cranberry bogs after harvest. Flemming said it is not certain that the chemical can cause cancer in human beings but that it was found to be carcinogenic after it was fed to rats which developed cancer of the thyroid.

According to the official, there was no evidence so far that cranberries grown in Wisconsin, New Jersey, and Massachusetts were contaminated, but an investigation was under way.

Some 3 million lb. of the berries are being buried in the northwest because of contamination. The action is being taken voluntarily by the National Cranberry Association.

Flemming noted that FDA has declined to set any tolerance level for any amount of a chemical in foods if the chemical produces cancer in animals. "The application of this principle is necessary in our opinion because, while in theory there may be a minute quantity of a carcinogen which is safe in foods, in actuality our scientists do not know whether this is true or how to establish a safe tolerance."

Some spokesmen for cranberry producers protested that Flemming's statement might ruin the market for cranberries during the holiday season. They said west coast cranberries are not shipped to the east and are strictly for western markets.

MISLEADING DENTIFRICE ADVERTISING HIT

Surgeon General Leroy E. Burney said the Public Health Service is in "complete accord" with the stand long taken by the American Dental Association against false and misleading statements in the advertising of dentifrices.

Although any enforcement action in this field is the responsibility of the Federal Trade Commission, "there are principles involved that are of direct concern to the Health, Education and Welfare Department in carrying out its own responsibilities," noted HEW Secretary Arthur S. Flemming.

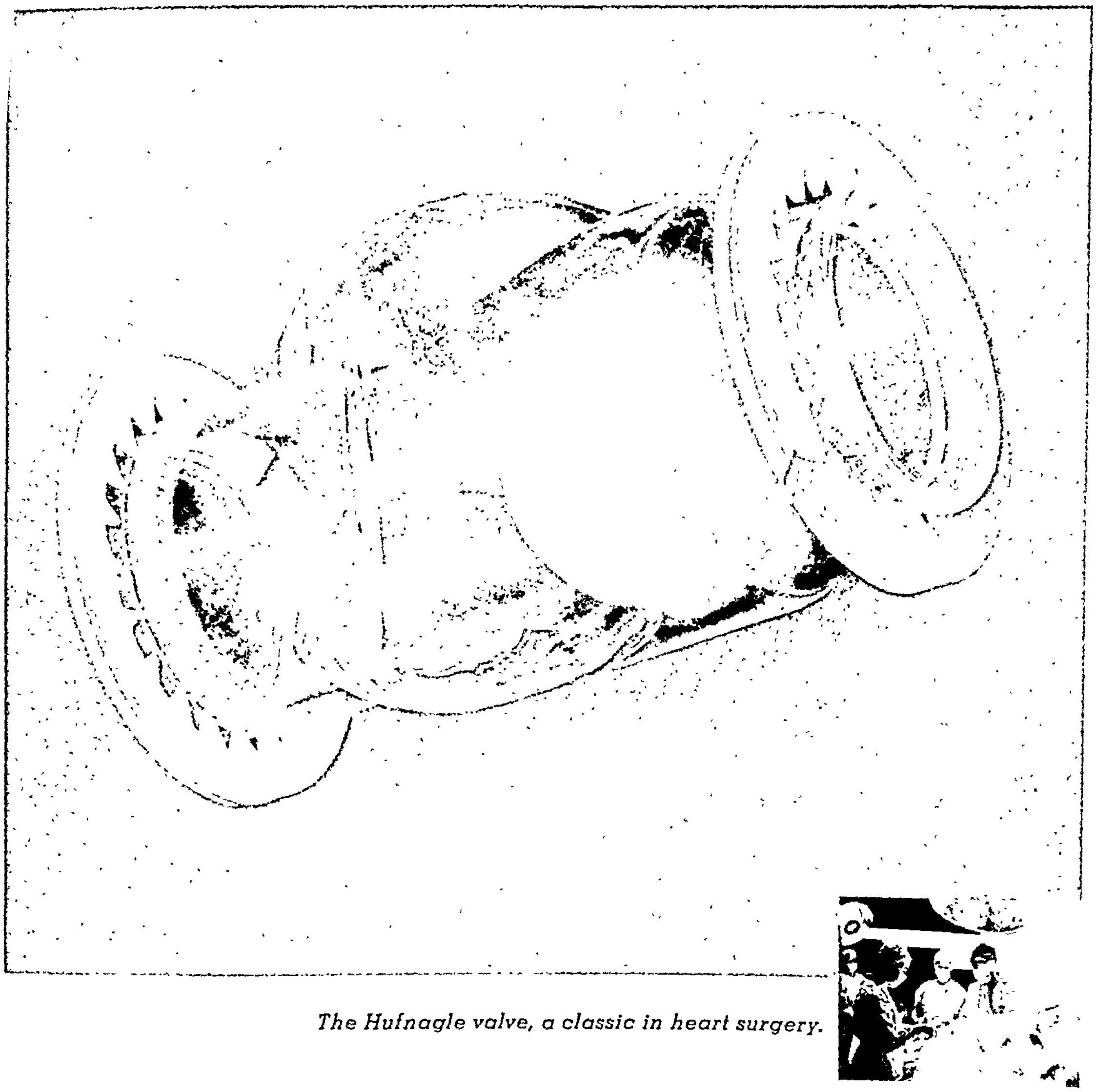
"People who believe the misleading advertising they hear and read and see—and who buy and use the product—may be lulled into a false sense of well-being and fail to obtain proper care from a dentist. Neglect of proper dental care, for whatever reason, sooner or later catches up with most people, and they find themselves with serious dental problems," Flemming said.

Dr. Burney pointed out that "while dentifrices are necessary for care of the teeth, they are primarily mechanical aids for cleaning them. No dentifrice in itself can prevent tooth decay or pyorrhea or any other disease. And no dentifrice can lighten the color of the teeth."

MISCELLANY

A Public Health Service national survey document, entitled "Children and Youth, Selected Health Characteristics," noted that young children suffered acute illnesses with twice the frequency of adults; that adults over 25 years of age averaged almost twice as many days of restricted activity from illness or injury; and that home accidents among children 15 years of age or under were the chief cause of injuries restricting activity or requiring medical attention.

FDA warned that the use of certain chemically treated diabetes test papers by women to determine the fertility cycle may be injurious and should be halted immediately. Some of these papers contain the chemical tolidine, "which has not been adequately tested for its effects on the sensitive tissues of the female reproductive system," the government said.



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SEARLE RESEARCH IN THE SERVICE OF MEDICINE

MEETINGS

AMERICAN MEDICAL ASSOCIATION: Dr. F. J. L. Blasingame, 535 North Dearborn St., Chicago 10. Executive Vice-President.
1959 Clinical Meeting, Dallas, Texas, Dec. 1-4.
1960 Annual Meeting, Miami Beach, Fla., June 13-17.
1960 Clinical Meeting, Washington, D. C., Nov. 29-Dec. 2.
1961 Annual Meeting, New York City, June 26-30.
1961 Clinical Meeting, Denver, Nov. 28-Dec. 1.
1962 Annual Meeting, Chicago, June.

AMERICAN

1959

November

American Academy for Cerebral Palsy, Statler Hilton Hotel, Los Angeles, Nov. 30-Dec. 2. Dr. Glidden L. Brooks, Brown University, Providence 12, R. I., Secretary.

American College of Chest Physicians, Dallas, Texas, Nov. 29-30. Mr. Murray Kornfeld, 112 E. Chestnut St., Chicago 11, Executive Secretary.

District of Columbia, Medical Society of, Statler-Hilton Hotel, Washington, D. C., Nov. 23-25. Mr. Theodore Wiprud, 1718 M Street, N. W., Washington 6, D. C.

International College of Surgeons, Second Western Regional Meeting, Stardust Hotel, Las Vegas, Nev., Nov. 22-24. Dr. F. M. Turnbull Jr., 1930 Wilshire Blvd., Los Angeles 57, Secretary-Treasurer.

Inter-Society Cytology Council, Statler-Hilton Hotel, Detroit, Nov. 19-21. Dr. Paul A. Younge, 1101 Beacon St., Brookline 46, Mass., Secretary-Treasurer.

National Society for Crippled Children and Adults, Palmer House, Chicago, Nov. 29-Dec. 2. Dr. Dean W. Roberts, 2023 W. Ogden Ave., Chicago 12, Executive Director.

Puerto Rico Medical Association, Santurce, Nov. 24-28. Mr. J. A. Sanchez, Box 9111, Santurce 29, Puerto Rico, Executive Secretary.

Southern Thoracic Surgical Association, Edgewater Gulf Hotel, Edgewater Park, Miss., Nov. 19-21. Dr. Hawley H. Seiler, 517 Bayshore Blvd., Tampa 6, Fla., Secretary.

Western Surgical Association, The Broadmoor, Colorado Springs, Colo., Nov. 19-21. Dr. John T. Reynolds, 612 N. Michigan Ave., Chicago 11, Secretary.

December

American Academy of Dermatology and Syphilology, Palmer House, Chicago, Dec. 5-10. Dr. Robert R. Kierland, First National Bank Bldg., Rochester, Minn., Secretary-Treasurer.

American Association for the Advancement of Science, Morrison Hotel, Chicago, Dec. 26-31. Mr. Sidney S. Negus, Medical Coll. of Virginia, Richmond, Va., Director of Public Information.

American Psychoanalytic Association, Biltmore Hotel, New York City, Dec. 4-6. Dr. David Beres, 151 Central Park West, New York 23, Secretary.

American Rheumatism Association, Henry Ford Hospital, Detroit, Michigan, Dec. 11. Gerard W. Speyer, 10 Columbus Circle, New York 19, Executive Secretary.

Association for Research in Nervous and Mental Disease, Inc., Hotel Roosevelt, New York City, Dec. 11-12. Dr. Rollo J. Masselink, 700 W. 168th St., New York 32, Secretary-Treasurer.

First Annual Graduate Medical Education Conference-Residency Training Program, Univ. of Pennsylvania, Philadelphia, Dec. 3-4. Dr. Alfred S. Frobese, Graduate School of Medicine, U. of Pennsylvania, Philadelphia 3, Chairman.

Medical Society of the United States & Mexico, Valley Ho Hotel, Scottsdale, Ariz., Dec. 2-4 (followed by two-day session Desert Inn, Las Vegas, Nev.). Dr. A. H. Tallakson, 2025 N. Central Ave., Phoenix, Ariz., Convention Co-Chairman.

New York Heart Association, Symposium on Salt and Water Metabolism, Biltmore Hotel, New York City, Dec. 11-12. Dr. Alfred P. Fishman, N. Y. Heart Association, 10 Columbus Circle, New York City, Chairman.

New York State Society of Anesthesiologists, Inc., Postgraduate Assembly in Anesthesiology, Hotel New Yorker, New York City, Dec. 9-12. Dr. Edwin J. DePolo, 131 W. 11th St., New York 11, Secretary.

1960

January

American Academy of Allergy, Hollywood Beach Hotel, Hollywood-by-the-Sea, Fla., Jan. 11-13. Mr. James O. Kelley, 756 N. Milwaukee St., Milwaukee 2, Wis., Executive Secretary.

American Academy of Orthopaedic Surgeons, The Palmer House, Chicago, Jan. 23-28. Mr. John K. Hart, 116 S. Michigan, Chicago 3, Executive Secretary.

American College of Surgeons, Sectional Meeting, the Brown Hotel, Louisville, Ky., Jan. 21-23. For information write: Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

Big Mountain Medical Meeting, Big Mountain Ski Resort, Whitefish, Mont., Jan. 20-30. Dr. George H. Gould, Kalispell, Mont., Chairman.

Northwest Society for Clinical Research, Seattle, Jan. 9. Dr. Jo R. Hogness, 721 Minor Ave., Seattle 4, Secretary-Treasurer.

Rocky Mountain Traumatic Surgical Society, Aspen, Colo., Jan. 30. Dr. Charles Houston, 420 Hyman St., Aspen, Colo., Execut Secretary.

Western Association of Physicians, Carmel, Calif., Jan. 27-29. Wade Volwiler, Dept. of Med., U. of Washington, Seattle 5, Secreta

Western Society for Clinical Research, Carmel-by-the-Sea, Cal Jan. 28-30. Dr. William N. Valentine, U. of California Medical Cen Dept. of Medicine, Los Angeles 24, Secretary.

February

Alaska State Medical Association, Anchorage, Feb. 18-20. Dr. Gec Hale, 501 "L" Street, Anchorage, Alaska, Chairman.

American Academy of Occupational Medicine, Williamsburg Williamsburg, Va., Feb. 10-12. Capt. Lloyd B. Shone, Bureau of Me cine and Surgery, Navy Dept., Washington 25, D. C., Secretary.

American College of Allergists, Inc., Americana Hotel, Bal Harb Miami Beach, Fla., Feb. 28-Mar. 5. Mr. Eloi Bauers, 2160 Rand Tow Minneapolis 2, Executive Vice-President.

American College of Radiology, Roosevelt Hotel, New Orleans, 3-6. Mr. William C. Stronach, 20 N. Wacker Dr., Chicago 6, Execu Director.

American College of Surgeons, Sectional Meeting for Surgeons Nurses, Statler Hilton, Boston, Feb. 29-Mar. 3. For information wr Dr. H. P. Saunders, 40 E. Erie St., Chicago 11.

American Orthopsychiatric Association, Inc., Sherman Hotel, Chic Feb. 25-27. Marion F. Langer, Ph.D., 1790 Broadway, New York Executive Secretary.

California Medical Association, Ambassador Hotel, Los Angeles, 21-24. Mr. John Hunton, 450 Sutter St., San Francisco 8, Exec Secretary.

Central Surgical Association, Drake Hotel, Chicago, Feb. 18 Dr. Angus D. McLachlin, Victoria Hospital, London, Ont., Can Secretary.

Congress on Medical Education and Licensure, Palmer House, cago, Feb. 7-9. For information write: Council on Medical Educa and Hospitals, American Medical Association, 535 N. Dearborn Chicago 10.

Mid-South Postgraduate Medical Assembly, Peabody Hotel, Mem Tenn., Feb. 9-12. Mr. Leslie H. Adams, 774 Adams Ave., Memph Tenn., Executive Secretary.

National Association of Methodist Hospitals and Homes, De Hilton Hotel, Columbus, Ohio, Feb. 16-18. Mr. Olin E. Oeschger, Rush St., Chicago 11, General Secretary.

Obstetrical and Gynecological Assembly of Southern Califor Los Angeles, Feb. 6-7. Dr. Kenneth Morgan, 1020 Wilshire Blvd., Angeles 57, Secretary.

Society of University Surgeons, Minneapolis, Feb. 11-13. Dr. Eiseman, 4200 E. Ninth Ave., Denver 20, Secretary.

Symposium on Fundamental Cancer Research (14th), Universit Texas, Houston, Feb. 25-27. For information write: University of T M. D. Anderson Hospital & Tumor Institute, Houston 25, Texas.

March

American Broncho-Esophagological Association, Deauville H Miami Beach, Fla., Mar. 15-16. Dr. F. Johnson Putney, 1712 Locust Philadelphia 3, Secretary.

American Academy of Forensic Sciences, Drake Hotel, Chic Mar. 3-5. Dr. W. J. R. Camp, 1853 W. Polk St., Chicago 12, Secret Treasurer.

American Academy of General Practice, Philadelphia, Mar. 19 Mr. Mac F. Cahal, Volker Blvd., at Brookside, Kansas City 12, Executive Director.

American Association for the History of Medicine, Inc., Charles S. C., Mar. 24-26. John B. Blake, Ph.D., c/o Smithsonian Institut Washington 25, D. C., Secretary.

American College of Surgeons, Sectional Meeting, The Broadm Colorado Springs, Colo., Mar. 21-23. For information write: Dr. H Saunders, 40 E. Erie St., Chicago 11.

American College of Surgeons, Sectional Meeting, Sheraton-Port Hotel, Portland, Ore., Mar. 28-30. For information write: Dr. H Saunders, 40 E. Erie St., Chicago 11.

American Gastroenterological Association, Roosevelt Hotel, Orleans, Mar. 31-Apr. 2. Dr. Wade Volwiler, Dept. of Med., Univ Washington, Seattle, Secretary.

American Gastroscopic Society, Roosevelt Hotel, New Orleans, Mar. Dr. Arthur M. Olsen, Mayo Clinic, Rochester, Minn., Secretary-Treas

American Laryngological Association, Deauville Hotel, Miami Be Fla., Mar. 18-19. Dr. Lyman Richards, Massachusetts Institute of Te nology, Cambridge 39, Mass., Secretary.

American Laryngological, Rhinological and Otological Soci Inc., Deauville Hotel, Miami Beach, Fla., Mar. 15-17. Dr. C. Ste Nash, 708 Medical Arts Bldg., Rochester 7, N. Y., Secretary.

American Otological Society, Deauville Hotel, Miami Beach, Mar. 13-14. Dr. Lawrence R. Boies, University Hospital, Minneap 14, Minn., Executive Secretary-Treasurer.

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CONTEMPORARY THERAPY OF THE MENOPAUSAL SYNDROME

Herbert S. Kupperman, M.D., Ph.D., Ben B. Wetchler, M.D.
and
Meyer H. G. Blatt, M.D., New York

Therapy for the postmenopausal patient has three aspects: psychotherapy, sedation, and hormonal therapy. A convenient index (menopausal index) for expressing the status of a patient is calculated by assigning to each of the 11 most common symptoms a weight factor and a severity coefficient; the sum of the 11 products ranges from 0 (for complete absence of menopausal symptoms) to about 35 (for serious distress). It was used as a criterion in comparing the efficacy of 27 types of treatment, including use of conjugated equine estrogens (299 cases), ethinyl estradiol (284 cases), and chlorotrianisene (124 cases). There are objections to the prolonged use of barbiturates, and the results obtained by the use of ataractic drugs alone in this study were but slightly better than those obtained with a placebo. Superior results were obtained with conjugated equine estrogens and ethinyl estradiol alone or when the latter was used with androgens. These effects were augmented with the addition of a phenothiazine compound to the estrogen-androgen combination. The judicious use of such therapy can afford relief from unnecessary discomfort to the ever-increasing number of menopausal women in the population.

NATURE has so endowed human beings that ovarian failure and incapacity for conception take place at an age when the potential for both fetal abnormalities and complications of pregnancy increases, simply on the basis of age. It has been said by some that the human female is the only species of her gender to live beyond the time that she can bear offspring.[1]

Why the ovary alone is singled out to become the "Achilles' heel"[2] of the glands of internal secretion is not understood. Beneficial as it may appear from the standpoint of eugenics or pure obstetrics, cessation of ovarian function does create certain disadvantages in many women. The usual age at which women cease to menstruate and are no longer able to bear children is between 45 to 50 years. Barnes[3] has stated that the age at cessation of menses has been extended during the last several hundred years. This comes as no surprise and might even be anticipated, when one considers that human vital statistics in general have shown an increase.

In fact, it is now estimated that in 1960 the 65-year-old age group will be about 10% of our population.[4] Thus, menopausal women will be encountered in larger numbers, and efforts must be made to make living more pleasant and worthwhile for them.

When the ovaries are no longer active not merely is fertilization impossible but an endocrine imbalance ensues. This disturbance may be productive of symptoms constituting the menopausal or cli-

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From the departments of obstetrics and gynecology and therapeutics, New York University–Bellevue Medical Center, and the Obstetric and Gynecologic Service (Third Division) and Endocrine Clinic (Fourth Division), Bellevue Hospital.

macteric syndrome. These symptoms need not be as sharply demarcated as the sudden cessation of menses but may be gradual in onset, giving rise imperceptibly to the full-blown clinical picture. On the other hand, the artificial menopause brought on by surgery or irradiation is apt to produce obvious effects more acutely, often in a matter of days, with vasomotor symptoms predominating.

Menopausal Physiology

Griffiths[5] has emphasized the extragenital value of the ovarian hormones. It is necessary to consider these physiological ramifications in any discussion of a therapeutic regimen organized to treat the menopause. The basis for this concept is that the ovary no longer can be considered primarily as a reproductive force; it has been shown to play an important role in metabolic function by virtue of its internal secretions. Estrogen, the prime endocrine secretion from the ovary, is essential in anabolism and nitrogen retention.[6] This is particularly true in the dynamic processes involved in calcification of bone. When the ovaries cease to function, and especially when they are surgically removed, it is likely that the stimulus for the osteoblastic activity is diminished so that normal bony matrix is reduced and decalcification results. As a consequence, osteoporosis occurs in some women and may be a serious cause of disability. It may progress to the extent of collapse of a vertebra. In addition, excessive excretion of calcium could result and be a factor in the formation of renal calculi.

Recent compilation of vital statistics has revealed some interesting findings, with evidence that coronary atherosclerosis is 10 to 40 times more prevalent in men under 40 than in women of a similar age.[7] However, the incidence of coronary heart disease associated with hypercholesteremia is comparable in postmenopausal women and in men of a similar age. It has been shown that high doses of estrogen can change an abnormal cholesterol pattern in men to a more favorable one and thereby diminish the degree of coronary insufficiency and extent of atherosclerosis.[8] In addition, it should be noted that patients subjected to bilateral oophorectomy are more vulnerable to hypercholesteremia than are women not so treated.

Animal experiments have shown that oophorectomy has been associated with adrenal hypertrophy. A similar situation has been said to exist in women in whom an increase in 17-ketosteroid excretion has been reported to occur in the menopause. The increased adrenocortical activity presumably occurring in the menopausal patient may theoretically predispose these patients to cardiovascular disease, as suggested by the work of Selye[9] on stress. Clinically the hypertensive phase noted in the climacteric patient is probably associated with the vasomotor instability that these patients exhibit. However, hypertension per se is not likely to appear in a previously normotensive female. Of a group of 200 women in the menopause, including 179 who were surgically castrated, 13% were hypertensive as compared to a 10% incidence of hypertension in the same group of women prior to the onset of the climacteric syndrome.[7]

Menopausal Index.—With the onset of the menopause follicle-stimulating hormone (FSH) may be excreted in large amounts, and the urinary estrogens levels are usually diminished. Assays to determine these changes are costly and cannot be considered as routine procedures. The vaginal smear is helpful but not absolute. At one time it was felt that the vaginal smear might be a possible yardstick to use in therapy. At the present time no definitive relationship has been found to exist among severity of symptoms, clinical response, and degree of cornification shown by the vaginal smear. Randall[10] found in patients with menopause of from 5 to 10 years' duration that 44.8% of the women with natural menopause showed estrogen deficiency; with hysterectomy and castration 30% more had deficient smears than after hysterectomy alone. Inasmuch as the laboratory and specific tests used in detecting hormonal insufficiency are too complicated and not precise enough to establish a diagnosis in women adequately, the clinician must depend on the symptoms of the climacteric to diagnose the condition in his patient.

The symptoms and not the laboratory data will also serve as more accurate criteria in determining the efficacy of therapy. At this point we will not take issue with the psychiatric or endocrine treatment of the menopause. However, suffice it to say that the combined psychiatric-endocrine approach to the treatment of the menopause will, no doubt, yield infinitely better therapeutic results than either one alone. Nevertheless, we do feel that the endocrine management of these patients as the principal form of therapy would offer the patient a more reasonable and simpler, yet efficacious, means of treatment. The principal handicap in determining the effectiveness of endocrine therapy is that in human beings, unlike animals, medication in general exerts a twofold effect, one due to the pharmacological action of the drug itself and the other to the psychological influence of drug administration. In order to determine more precisely the therapeutic responsiveness of the menopausal patient to a hormonal or nonhormonal agent we have devised an objective means of evaluation, whereby certain of the most prominent symptoms of the climacteric are used in formulating a numerical conversion index, designated as the menopausal index. This provides an effective means of determining the relative potential of any therapeutic agent in the control of the menopausal patient. We have based our evaluation of drug therapy in the menopause on the effect of the preparation to be tested on the changes noted in the 11 most common symptoms seen in the menopausal patient.

In the past decade this system has offered a most objective means of studying the effect of hormone or drug therapy in the menopausal patient. Each symptom is given a numerical value, ranging from 1 to 4; the more important the symptom, the higher the figure between 1 and 4. In addition, the severity of the symptoms referable to the specific complaint is also given a numerical conversion factor, ranging from 0 to 3. The factor referable to the symptom is then multiplied by the factor referable to its severity. In so doing one obtains an arbitrary figure or product representative of the severity for that particular complaint. The sum total of all these products furnishes us with a figure which is referred to as the menopausal index (table 1). Moreover, the following facts must be stated to further substantiate this mode of evaluation. The severity of the symptoms as noted above, ranging from 0 to 3, is obtained as follows: If the patient had no complaints, on interrogation for a specific symptom, this is graded as 0. This zero multiplied by the numerical conversion factor of the particular complaint yields 0; therefore, this symptom obviously does not contribute to the sum or menopausal index. If the patient complains of mild symptoms a factor of 1 is given; if the patient complains of moderate symptoms, a factor of 2 is given; and if the symptoms are severe, the factor is 3.

Except for vasomotor symptoms, paresthesia, insomnia, and nervousness (table 1) the symptoms are all given a numerical conversion factor of 1. These four symptoms we believe are most prominent and cause the patient the greatest difficulty. Vasomotor symptoms exceed the others in importance and are usually responsible for bringing the patient to the attention of the physician; hence, they are given a numerical conversion factor of 4. Paresthesia, insomnia, and nervousness, less important than the vasomotor symptoms but of greater importance than the remaining symptoms, are given a factor of 2. Thus, if a patient has severe vasomotor symptoms, the numerical conversion factor 4 is multiplied by the severity factor of 3, giving a factor of 12, which would thus increase the total menopausal index. If the clinician depends primarily on vasomotor complaints for determination of the need for therapy, he neglects a large group of patients who are suffering with other manifestations of the menopause yet who have minimal vasomotor symptoms.

At this point we would like to emphasize that "hot flushes" are a comparatively late manifestation in the climacteric syndrome. Basically, it has been said that the arteriolar changes of the blush area result from diminution or absence of steroid control. Reynolds [11] has shown that the loss of this regulator causes hot flushes by vasomotor instability. Patients with severe cases may be plagued primarily with abundant perspiration and chilly sensations. One patient described her difficulty as "like walking out and standing in the rain." Suddenly her face was covered with sweat, and yet no heat was experienced. These vasomotor complaints may vary from transient feelings of warmth that are infrequent to objective evidence of reddening. It must also be borne in mind that exciting factors such as a large meal, joy, anger, or even the normal vascular changes that occur from relaxation in sleep are factors that may influence the frequency and severity of vasomotor symptom reactions.

The physician who is acutely aware of the climacteric syndrome would suspect its presence in a patient complaining of arthralgia, myalgia, formication, headache, and palpitations, despite the fact that vasomotor symptoms might be minimal or absent and menses continue. The so-called lesser symptoms, when present in sufficient numbers, may be equally as distressing as vasomotor symptoms and warn the clinician of the impending climacteric syndrome. We feel, therefore, that the entire menopausal symptomatology must be considered *in toto* both in diagnosis and in measurement of the effectiveness of drug therapy.

TABLE 1.—*Derivation of Menopausal Index*

Symptom	Factor	Severity*	Numerical Conversion†
Vasomotor	4	M	8
Paresthesia	2	+	6
Insomnia	2	+	6
Nervousness	2	M	4
Melancholia	1	+	3
Vertigo	1	S	1
Weakness (fatigue)	1	S	1
Arthralgia and myalgia	1	M	2
Headache	1	S	1
Palpitation	1	+	3
Formication	1	0	0
Menopausal index (sum)‡			35

* 0 = none = 0; S = slight = 1; M = moderate = 2; + = marked = 3.
† Numerical conversion = factor × severity.
‡ Severe = 35+; moderate = 20-35; mild = 15-20.

With use of the above scheme we have observed that a patient with severe menopausal symptoms usually has a menopausal index of 35 or more. A moderate menopausal syndrome would be noted in a patient with an index of between 20 and 35, while the patient with mild menopausal symptoms would have an index of around 15. If the therapeutic regimen is efficacious, it should reduce the index to a level of 15 or less. This system is simple and, while purely arbitrary, has been of tremendous value in the study of drugs for the treatment of the menopause. However, in an attempt to be more objective in the evaluation of therapy in the menopausal patient, with use of the menopausal index, we have adopted a "blind" testing system of evaluating drug therapy. This system involves the administration of drugs to the patient by a physician who does not know which drug is being administered (the patient also does not know what drug she is receiving). The patient is usually interrogated by the same doctor or group of doctors; to avoid the need of acquainting a new physician with the system involved. Furthermore, the medicament is dispensed by a nurse by code number, so that the physician cannot be aware of what medicament is being dispensed and does not know whether the patient is receiving a placebo or the active preparation being tested.

It is important to emphasize that adequate rapport between the physician and the patient is necessary. At the same time it should be mentioned that these factors are, in all probability, invariably constant, and any psychological overplay involved would not alter the patient's response to any of the medicaments being ingested. Placebo therapy is employed freely and intermittently with whatever active preparation is being tested at the time. It should be noted, too, that the so-called placebo reactors were not used in the evaluation of hormonal therapy. In other words, those patients showing an adequate response to a placebo cannot be considered as true menopausal patients and hence were not used in the evaluation of drug therapy. In the process of evaluation the patient received different preparations at four-week to six-week intervals, after which the response to each drug was evaluated by the menopausal index as well as by clinical evaluation of the patient herself. This included interrogation of the patient about the effectiveness of the preparation as compared to previous medicament which she received. When these data were tabulated the menopausal index was obtained, and further therapy was determined by this specific response.

The word "placebo" is not used in our clinic, but the word "obecalp" has been coined. "Obecalp" is placebo spelled backwards, so that when this term is used the patient is not aware that she is being tested for the veracity of her statement or symptom-complex in general. "Obecalp" in our hands has proved to be effective in approximately one-third of our patients. We feel that some of the dramatic results achieved with preparations such as vitamin E and a famous vegetable compound now on the market must be attributed to the psychological effect of a placebo rather than to any therapeutic action of the medicament itself.

Before therapy is discussed, several points should be emphasized with respect to proper interrogation of the patient. For example, we attach a considerable degree of importance to the symptoms of a patient who claims that vasomotor symptoms, occurring at night, disturb her sleep. These differ from the vasomotor symptoms which are seen in the hypertensive patient during the daytime. A hypertensive patient who is not menopausal may experience flushes but they are not the true vasomotor symptoms of a menopause, inasmuch as when the hypertensive patient sleeps she is not disturbed by the hypertensive flushes or flushing which she previously had noted during the day. The question of palpitations should also be looked into more deeply. The patient should not merely be asked whether there is a quickening or acceleration of her heartbeat but, specifically, whether she observes palpitations in a sitting or resting position. This is true palpitation and is not related to activity.

The physician must be circumspect in his questioning and be aware that certain family and economic problems may enhance or diminish the menopausal symptoms. It is patients with these problems in whom we feel that the clinical evaluation and clinical impression are as important as the menopausal index.

Therapy

The therapeutic approach to the menopausal patient can be placed under three categories; namely, psychotherapy, sedation, and hormonal treatment. One must emphasize that not all women, when they undergo cessation of menses, experience menopausal symptoms. We feel that it is also difficult to evaluate precisely the number of women who experience vasomotor symptoms as compared to those who do not. A report[12] has shown that in 1,000 cases studied 50.8% of patients had no symptoms except cessation of menses. Of those who did have symptoms 89.7% worked as usual without interruption, and only 10.3% were truly incapacitated at intervals. This does not mean that the remaining patients, the 89.7% who worked as usual, did not have menopausal symptoms. A patient may work with vasomotor symptoms or she may not work, depending on her character. It should be emphasized that drug therapy, psychotherapy, and sedation are reserved only for those patients who request treatment. The fact that the patients are able to perform their household duties and are not completely incapacitated does not preclude the therapeutic use of whatever agent the physician finds helpful.

Psychotherapy.—If psychotherapy includes kindly treatment of the patient and a truly sympathetic reception of her complaints, it may be readily offered and frequently given. However, psychotherapy may be limited in the minds of certain physicians to the so-called couch treatment. This type of therapy is usually inappropriate and is inaccessible to most patients, especially those in the lower economic strata. There is, however, no question that even minimal psychotherapy, when used in conjunction with the therapeutic armamentarium mentioned below, will be effective in allaying many of the menopausal symptoms.

Information not easily obtained yet which may influence a patient's response to therapy concerns eating habits, especially if the patient is a widow and lives alone. Such patients often do not think food is important, and dietary deficiencies occur. Also, seven nights a week spent glued to the television set are not relaxing. Clinic patients, notably those who work, would do well with a few suggestions on the allocation of a little time to a few simple diversions. In a large family the assistance of one of the children or the husband will easily solve problems that the patient herself is apt not to appreciate. This may considerably improve the patient's mental status and thereby prevent an exacerbation of the menopausal syndrome.

Sedation.—A word of caution should be expressed about the use of phenobarbital continuously and for prolonged periods of time. We know that more than 24 hours are required before a single dose of phenobarbital may be excreted from the body. Hence, the possibility of cumulative effects of phenobarbital ingestion must be recognized, and barbiturate addiction does take place. One can conceivably anticipate that a patient who is so addicted may show symptoms not unlike those noted in the climacteric, despite the fact that barbiturate therapy is continued without cessation. If the patient becomes addicted to phenobarbital, the need for further and additional therapy is evident. As a result, one may create a symptom complex similar to a rolling snowball whereby the addition of more therapy requires more of the same drug, because of habituation, so that the patient may be condemned to the use of continuous phenobarbital therapy per se. Thus, we feel that the continued use of phenobarbital without restriction may lead, at times, to the undesirable side-effect of barbiturate addiction. Such a result would make the treatment worse than the disease.

In an attempt to overcome some of the undesirable side-effects of phenobarbital administration, a number of ataractic compounds have been tested in the menopausal patient. These have included perphenazine, meprobamate, hydroxyzine, ectylurea, and benactyzine. The data indicated that the use of these compounds in adequate doses did not seem to be therapeutically successful in controlling the climacteric syndrome, on the basis of their failure to alter the menopausal index. As a matter of fact, benactyzine therapy gave results considerably poorer than placebo therapy. This was due to the undesirable side-effects attributed to the administration of the preparation itself. In general, the results with the other ataractic drugs indicated that they were no better than those obtained with phenobarbital and slightly better than that obtained with a placebo.

Hormonal Therapy.—The specific therapy used included (1) estrogens, (2) estrogens and androgens, (3) androgens alone, and (4) estrogens in conjunction with tranquilizers or sedatives. These may be administered (1) orally, (2) by injection, (3) by pellet implantation, (4) vaginally, or (5) by inunction. In our initial efforts[13] to determine the results of medication in the climacteric we used both synthetic estrogens and the so-called steroidal groups. The synthetics included diethylstilbestrol (Stilbestrol), hexestrol, dienestrol, methallenestril (Vallestril), and chlorotrianisene. The steroidal estrogens included free estradiol, ethinyl estradiol (Estinyl), conjugated equine estrogens (Premarin), estrone, estradiol linguets, and a combination of free and ethinyl estradiol or conjugated equine estrogens, with and without methyltestosterone.

In addition, we employed piperazine estrone sulfate, potassium estrone sulfate, crystalline estrone sulfate, and crystalline estrone sulfate, enteric-coated. Vitamin E preparations, phenobarbital, and placebos were given from time to time with the above estrogenic compounds, with attention to the appearance of the preparation in order that the patient should receive no hint of change of medicament.

TABLE 2.—*Effect of Endocrine and Nonendocrine Preparations on Patients with the Menopausal Syndrome*

				Results		
No.	Preparation	Daily Dose, Mg.	Patients, No.	Excellent	Moderate	Poor
1	*Placebo*	*1 tablet*	735	171	126	438
2	Phenobarbital	15 t.i.d.	117	25	27	65
3	Conjugated equine estrogens	1.25	299	206	68	25
4	Ethinyl estradiol	0.05	284	171	71	42
5	Estrone	10,000 I.U.	86	36	24	26
		0.5	36	13	11	12
6	Estradiol	1.0	38	20	13	5
7	Estradiol linguets	0.25	29	15	11	3
8	Stilbestrol	0.1 t.i.d.	49	15	15	19
9	Dienestrol	0.5	91	28	32	31
10	Hexestrol	3.0	48	14	14	20
11	Chlorotrianisene	12*	124	61	40	23
12	Methallenestril	3	95	38	29	28
13	Methallenestril	3 b.i.d.	33	12	8	13
14	Ethinyl estradiol and methyltestosterone	0.02 5	114	53	38	23
15	Ethinyl estradiol and methyltestosterone	0.04 10	54	24	23	7
16	Ethinyl estradiol Methyltestosterone Perphenazine	0.04 10 4	97	57	29	11
17	Perphenazine	4	55	12	12	31
18	Potassium estrone sulfate	1.25	94	47	28	19
19	Piperazine estrone sulfate	1.5	75	44	21	10
20	Estrone sulfate	1.25	82	42	21	19
21	Estrone sulfate, enteric-coated	1.25	78	35	28	15
22	Meprobamate	400 q.i.d.	41	11	8	22
23	Hydroxyzine	10 t.i.d.	22	2	4	16
24	Hydroxyzine	25 b.i.d.	29	7	7	15
25	Ectylurea	300 t.i.d.	55	7	16	32
26	Benactyzine hydrochloride	2.5 t.i.d.	14	2	1	11
27	Benactyzine hydrochloride	5 t.i.d.	11	...	3	8

* or 24 mg. every other day

The dosages of the various preparations employed are listed in table 2. Vitamin E was provided in 50-100 mg. capsules or tablets daily. The bases for the responses noted in table 2 are clinical improvement and the menopausal index. This offered a more precise picture of the clinical response, in contrast to attempted evaluation based on the recording of the number of flushes in a

24-hour period, as recommended by Jones.[14] The vaginal smear, taken prior to each patient interview, could not be depended on for true grading of response. It may only be said that cornification was noted in most patients receiving estrogen therapy. We simply graded the clinical response as either excellent, associated with complete relief or moderate relief with minimal residual symptoms, or poor, with no relief being noted. The best results were obtained with ethinyl estradiol and conjugated equine estrogens alone or in combination with androgens. The crystalline estrone sulfate derivatives did not produce results as good as the conjugated equine estrogens, dose for dose. Stilbestrol produced nausea in 20% of cases. The frequency of this complaint definitely limited its use. The conjugated equine estrogens were presumed to be the source of two cases of dermatitis. Withdrawal bleeding affected 18% of those receiving combined free and ethinyl estradiol.

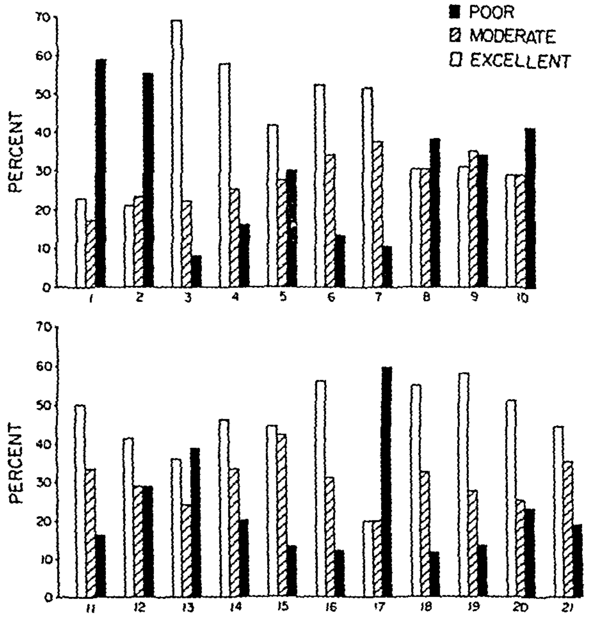

Fig. 1.—Effects of endocrine and nonendocrine preparations (numbers correspond to those in table 2) on patients with menopausal syndrome.

The graphic presentation in figure 1 shows that no one preparation could be considered perfect. None was 100% effective. Vitamin E, considered a panacea for so many conditions, did no better than a placebo. One other comment to be made about estrogen therapy is that it has been claimed that certain estrogens have less of a bleeding effect on the endometrium than others. We believe that when a comparable dose of an estrogen is used it has the same potential hazard of producing endometrial bleeding as any other estrogen. The purported results showing that certain preparations have less bleeding tendency may be explained simply by the fact that a less effective dose of that particular estrogen was being used. When a dose of any estrogen comparable to the clinical effectiveness of 0.05 mg. of ethinyl estradiol was used, the same bleeding tendency would occur.

When androgens, in the form of methyltestosterone, were added to the estrogens, physical vigor and *joie de vivre* became noticeable. Dull personalities seemed to become a bit less so. Occasionally, patients who had been coming to us for some time modestly whispered about an increase in libido. There were some, however, who did complain of distinct, bothersome clitoral irritation.

The apparent synergism of combined steroid therapy permitted us to give smaller doses of each substance used and yet anticipate an equal or greater effect than when comparable doses were used individually. Vaginal bleeding did not occur. We were constantly alert for masculinizing effects, but there was no evidence of arrhenomimetic phenomena of significance.

The general degree of improvement in a patient's well-being attributable to androgen therapy had a decided effect in ameliorating the anxieties and nervousness of which she originally complained. Estrogen therapy alone did not seem to us to be so all-inclusive in effect.

The physiological explanation of the clinical success of this combined steroid medication is perhaps closely related to the protein anabolism and maintenance of nitrogen and phosphorus balance, as well as body electrolytes and creatinine utilization that estrogens and androgens induce. Osteoporosis of the menopause is thus controlled. Although the true locale of the specific effect of testosterone is unknown, the estrogenic stimulus may be ascribed to favoring improvement in cell permeability.[5] It is reasoned then that, with the basic anabolic property of testosterone and the resultant protein storage, the enhanced cellular activity produced by estrogen increases the potential of the protein anabolic effect of the androgen. The over-all effect of estrogen-androgen combination is to prevent the depletion of body protein substances as age increases. Beyond the scope of this paper one must give serious consideration to long-range steroid therapy in geriatrics, as so well presented by Masters.[1] In his hands this regimen effectively influenced 75% of the persons treated, with notable physical and psychological improvement. We are entirely in accord with Masters' concepts and have confirmed his observations.

It should be mentioned that in the combined use of estrogens and androgens we do not mean to imply that estrogens can neutralize the undesirable effects of androgens and vice versa. The advantage of their combined administration lies in the fact that smaller doses of either one may be used, so that the combination of the two may produce a synergistic effect, approaching the effectiveness of either one alone when administered in higher doses. In other words, if a patient would bleed when 0.05 mg. of ethinyl estradiol per day was administered we could not prevent that bleeding by the addition of 10 mg. of methyltestosterone. On the other hand, if 10 mg. of methyltestosterone will produce beard growth in a woman, we cannot inhibit this hypertrichosis with a dose of 0.05 mg. of ethinyl estradiol. One can, however, diminish the dose of ethinyl estradiol to 0.02 mg. and administer 5 mg. of methyltestosterone simultaneously and achieve a therapeutic effect comparable to that obtained with 0.05 mg. of ethinyl estradiol. In so doing one diminishes the bleeding propensity which was observed when the 0.05-mg. dose of ethinyl estradiol was employed or the hirsutism noted with 10 mg. of methyltestosterone. An interesting possible advantage of therapy with estrogens and androgens combined is that the estrogens at times may promote fluid accumulation and induce increased nervousness, anxiety, and irritability in certain menopausal patients. The value of estrogens and androgens in these patients would be that the tendency for estrogens to produce enhanced nervousness is diminished with a smaller dose of estrogens, but the clinical efficacy is maintained by the addition of androgens without diminishing the desired clinical effect.

Table 3.—*Effect of Combined Therapy with Reserpine and Different Steroids on Patients with the Menopausal Syndrome*

Regimen*				Results		
No.	Preparation	Dosage, Mg.	Patients, No.	Excellent	Moderate	Poor
1	Reserpine ethinyl estradiol	0.1 0.02	43	12	11	20
2	Reserpine ethinyl estradiol	0.2 0.02	25	12	3	10
3	Reserpine methyltestosterone	0.2 5.0	35	15	9	11
4	Reserpine ethinyl estradiol methyltestosterone	0.2 0.02 5.0	57	29	11	17
5	Reserpine ethinyl estradiol methyltestosterone	0.1 0.01 2.5	50	20	14	16
6	Reserpine d-amphetamine homatropine methyl bromide	0.25 5.0 5.0	45	7	9	29

* *All preparations were administered b.i.d.*

A bit fearful of the possibilities of accumulation or addiction of extended barbiturate administration, we did not use the combination of estrogen and a barbiturate. Instead we attempted to determine clinically the value of combinations of reserpine,[15] the purified alkaloid prepared from Rauwolfia serpentina, with different hormones. Women with natural or surgically produced menopause who had demonstrated their capacities to respond to the preparations mentioned above were studied. Two clinically proved effective estrogens were administered, since a clinical response could be anticipated for the prescribed estrogen. Thereby one could ascertain the synergistic effect, if any, due to the addition of reserpine. The two estrogenic preparations were ethinyl estradiol, 0.05 mg. per day, and conjugated estrogens, 1.25 mg. per day. Basically both of these estrogens generally effected a 70 to 90% relief of symptoms. Smaller doses of either estrogen when combined with reserpine were found to be less satisfactory than the steroid alone. There is no synergistic action between reserpine and estrogen such as that noted between androgens and estrogen. On the other hand, complaints not attributable to the menopause but nevertheless apt to increase the severity of the symptomatology took origin in the side-effects from the reserpine. We encountered nasal stuffiness, drowsiness, unusual dreams verging on nightmares, and even Parkinson-like disorders.

The dose of reserpine was either 0.1 or 0.2 mg. twice daily. Such a fixed combination of reserpine and an estrogen was found to be somewhat of a handicap. It was apparent that when one component is productive of some untoward response an attempt at regulation is hindered by an inflexible combination. Nasal stuffiness and drowsiness, the most bothersome side-effects, treated also with amphetamine derivatives or homatropine methyl bromide, did not bring much relief in the presence of continued use of reserpine. Libido was not affected either favorably or unfavorably by reserpine. Table 3 shows the doses and types of preparations employed in combination with reserpine.

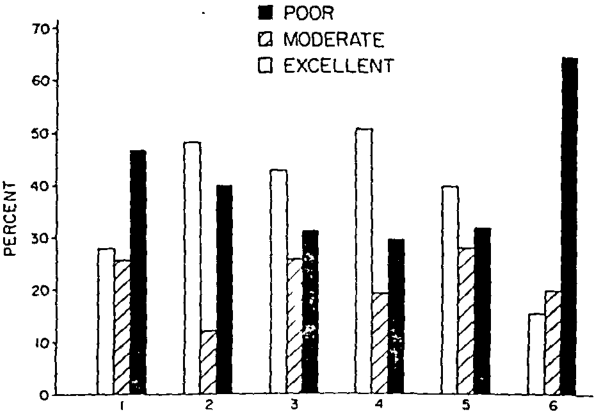

Fig. 2.—Effects of reserpine plus different steroids (numbers correspond to those in table 3) on patients with menopausal syndrome.

These data are graphically presented in fig. 2 and provide strong evidence for the fact that no set of combinations superseded the excellent results achieved with conjugated estrogens or ethinyl estradiol (table 2 and fig. 1). However, it should be emphasized that, if they are separately administered, the simultaneous use of steroids and reserpine may be helpful. A combined tablet did not seem advisable in our patients, because of inflexibility of dosage and undesirable effects due to the reserpine itself.

On the other hand, a combination of estrogen or estrogen and androgen with a phenothiazine compound seemed to be unusually effective in therapy of the climacteric syndrome. Administration of perphenazine with ethinyl estradiol and methyltestosterone, in the form of a delayed-absorption tablet, appeared to yield a better therapeutic effect than any one of the preparations administered alone (table 2 and fig. 1). No undesirable effects were observed, with the doses employed. There was no evidence that perphenazine alone or in combination induced or accentuated melancholia or depression in the patients studied.

TABLE 4.—*Effect of Parenterally Given Steroids on Patients with the Menopausal Syndrome*

No.	Preparation	Dosage, Mg. Given Every 2 Wk.	Patients, No.	Results		
				Excellent	Moderate	Poor
1	Estradiol cyclopentylpropionate	5	51	33	6	12
2	Estradiol valerate	10	106	71	24	11
3	Estradiol valerate	10*	16	6	6	4
4	Estradiol cyclopentylpropionate, ... testosterone cyclopentylpropionate	2 50	29	16	9	4
5	Estradiol cyclopentylpropionate, ... testosterone cyclopentylpropionate	2 100	68	48	13	7
6	Testosterone cyclopentylpropionate	100	28	18	5	5
7	Polyestradiol phosphate	40	41	24	7	10
8	Placebo	1 cc.	164	51	30	83

* Given every 3 wk.

Mode of Administration

Traditionally medicaments are most simply and safely administered orally. We found this means of therapy to be a noncomplicated and convenient mode in the majority of patients studied. Admittedly this requires repeated clinic visits for the medication, but it did permit a constant supervision of therapy and provided a means of varying the type and frequency of administration to judge adequately the clinical efficacy of the compounds studied. However, some patients did not take the prescribed tablets as ordered; and to assure a more precise observation all patients were requested to return the unused medicaments. Intramuscular injections were elected for patients who would not or could not remember to take the oral medicaments as given. In some this renewed confidence in the clinician, in cases in which a previous medicament did not completely satisfy. In evaluating several preparations we used the menopausal index technique to judge the duration of activity of preparations with relatively prolonged activity. We felt that these preparations had much to offer by providing a continuous and effective control of the patient's condition. Aqueous suspensions were not satisfactory because they were usually painful. In contrast, esterification of some steroids gave us nonirritating, oil-soluble materials that acted over a comparatively long period of time. Two such preparations were used—estradiol valerate (Delestrogen) and estradiol (Depo-Estradiol) cyclopentylpropionate.[16]

Table 4 and figure 3 show the control afforded by these parenterally given medicaments as compared to orally taken preparations listed. All of the long-acting preparations were clinically comparable, with respect to their ability to effect relief of menopausal symptoms. Parenterally given placebos, on the other hand, induced a poor effect by comparison. The outstanding result of the long-acting parenterally given medicaments was that relief lasted between 15 to 25 days. These results were encouraging since one could now offer intramuscular administration at two-week to three-week intervals, instead of the tedious and bothersome weekly or twice weekly administration previously practiced. Estradiol valerate, 10 mg., and estradiol cyclopentylpropionate, 5 mg., given usually at two-week intervals, were equally valuable and measured up well to the best results achieved with any of the orally given materials used. Good control for prolonged periods was obtained with these oil-soluble esters of estrogen. *For those patients in whom oil solutions were poorly tolerated an aqueous solution of polyestradiol phosphate proved to be an* effective substitute. Adequate control of the menopausal syndrome was achieved with 40 mg. of this preparation injected every two weeks. Oily and aqueous solution of the long-acting steroid could conveniently be used in patients who cannot swallow pills or tablets. The long-acting parenterally given medicaments provide a method of definitively controlling unreliable patients and add an additional approach to improve the therapeutic effect of steroid therapy in patients who do not respond adequately to oral medication.

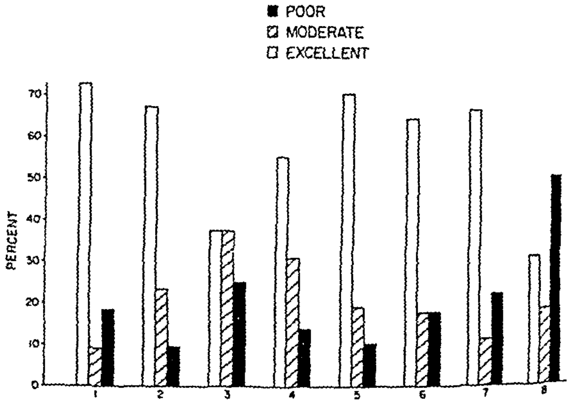

Fig. 3.—Effects of parenterally given steroids (numbers correspond to those in table 4) on patients with menopausal syndrome.

Despite the simplicity of oral medication and the availability of parenterally given steroids, which may offer relief for longer periods of time, we found that the menopause induced by surgery is best treated by pellet implantation. Deansley and Parkes[17] showed that pellet implantation of steroids resulted in a prolonged release of the material in a manner akin to that observed in the natural steroid secretion from the organs of internal secretion. The advantages of this type of therapy were a sustained, continuous physiological level of the implanted steroid substance over an extended period of time. Therefore, in humans, pellet implantation was seen as a way of offering the patient untold comfort due to the long-continued effect of pellets. We believe that they proved the ultimate aim in replacement therapy, inasmuch as continued maintenance of beneficial levels of the steroids is achieved with as little bother to the patient as possible. Not only would one get a continuous endocrine effect but the pellet itself would in substance duplicate the secretion of the ablated organ.

The surgically induced menopause may frequently be apparent before the patient leaves the hospital. This is especially true of younger women, certainly in those below the age of 40. Of necessity, one would anticipate a relatively longer and possibly more difficult time in treating these castrated women. It is a real challenge to treat this type of patient successfully, without making therapy at this early age a burdensome matter. The same reasoning may be applied even to older patients who are suddenly deprived of ovaries that are gradually declining in function.

It is impossible at this point to proceed without a word about the practice of oophorectomy dependent on age alone. We go along with Randall's[18] strong plea to retain ovaries in the absence of any pelvic disease that makes it imperative to remove these important structures. The present trend does seem to oppose the routine bilateral oophorectomy of normal ovaries, in cases of benign uterine disease, just because of age. This strikes a happy note, since in time the frequency of surgically induced menopause must proportionately lessen.

In treating patients who had both ovaries removed at the time of total abdominal hysterectomy we have found it extremely effective to insert pellets of steroid hormone into the rectus muscle beneath the anterior sheath during closure of the abdominal wall. As a rule, we have avoided pellet implantation in patients with breast disease or a history of genital carcinoma.

Our earlier studies[19] included at first the implantation of single 25-mg. pellets of estradiol. This was quickly increased to three pellets of 25 mg. of the same substance. Now we use three pellets of 25 mg. of estradiol and two pellets of 75 mg. each of testosterone propionate.

Initially we studied a group of surgically castrated women treated with estradiol pellets alone and used as controls a corresponding number of castrated women who were not receiving these pellets. The menopausal index showed effective control and reduction in severity of complaints up to 15 months. However, not all of the patients receiving pellets were relieved of all symptoms, and not all of the surgically castrated patients in the control series complained of menopausal symptoms. As in the case of a young municipal hospital patient with huge fibroids and pelvic inflammatory disease treated with total abdominal hysterectomy and bilateral salpingoophorectomy, one may occasionally encounter women who have complete absence of menopausal complaints. We believe, however, that in view of the majority of women in the younger age group, i. e., under 40 years of age, who exhibit profound and incapacitating symptoms after bilateral oophorectomy with total hysterectomy, that implantation of estrogens or estrogens combined with androgens is a propitious and wise form of therapy. We would like to emphasize that pellet implantation of estrogens is contraindicated in any patient who has a uterus or ovaries. The vaginal smears provided evidence for the long-continued effects of the pellets, inasmuch as many of the patients showed a normal or increased degree of cornification 12 to 15 months after surgery and implantation. As a rule the estrogenic effect was promptly noted, but occasionally smears did not manifest an effect of the pellets for the first six weeks. Breast congestion was not noted in any of our patients receiving therapy with estrogens alone or in those in whom estradiol and testosterone pellets were implanted.

Estrogen pellets may cause irregular bleeding, if the uterus remains in situ, as has been reported in from 30 to 50% of the cases. Small fibroids in these uteri have increased in size. Twombly and Millen[20] advised that an intact uterus is a contraindication to estradiol pellet implantation unless prior sterilization by radiation had been done. We encountered no vaginal spotting (not unexpectedly, as every one of our patients had had a hysterectomy). Originally it was felt that estrogen pellets alone induced a smooth course, free of the postoperative symptoms usually noted in precipitous estrogen withdrawal. It was also noted that in the control series we had many minor complaints, notably absent in the patients treated with estrogen pellet implantation. Accordingly, we permitted ourselves to assume that the lesser difficulties were relieved in the patients treated with pellets. It is possible that the symptoms might not have necessitated medical aid, but still they would have been a burden to the patient.

Dispelling such complaints with pellet implantation offers the physician a valuable tool in the treatment of surgically induced climacteric. The addition of testosterone pellets to the estrogen was distinctly advantageous in offering the patient a general sense of well-being. While the estrogen alone produced a well-controlled and satisfied patient, the combination of androgen and estrogen pellets gave a more effective response; improved spirits were readily apparent, as well as enhanced libido, an important factor in maintaining normal marital relationships. In these cases we were careful to note any evidence of excessive hair growth. The slow release of androgens from the pellet site in doses of gammas per day could not be considered a factor in hirsutism. We are all cognizant of the increased hirsutism that may spontaneously occur in some postmenopausal women. However, we take issue with those who believe that the minute amounts of androgens released from the pellet site may cause hirsutism. Any hair growth noted is probably a consequence of the natural course of the syndrome. When for some reason pellets were not implanted at operation, we utilized the trochar insertion for implantation. This technique when done properly is not associated with significant discomfort and should be considered essentially an office procedure. The subscapular or inguinal regions may be used. The same number of pellets are implanted as were used at the time of surgery, and the hia'us created is closed with a single 0000 suture.

A relatively infrequent site for the administration of steroids is the vagina. Nonetheless, this mode of therapy may be of tremendous value in patients who have developed senile vaginitis. It is these patients who are especially prone to show loss of elasticity and atrophic local vascular changes conducive to the formation of fissures. Often this results in the appearance of bleeding areas and a bloody discharge. When this occurs in patients well past the menopause, not only is it a source of mental anguish but it is associated with marked physical discomfort. These lesions responded well to local application of estrogenic creams or suppositories. Of course, adequate testing by smear or biopsy may be indicated to rule out the factor of neoplasm. The creams that may be utilized with effectiveness should contain 0.05 mg. of diethylstilbestrol, 0.5 mg. of dienestrol, or 1.25 mg. of conjugated equine estrogens per gram of ointment. The local use of these estrogens is associated with prompt relief and usually does not cause any systemic effect. Unfortunately, dyspareunia and pruritus vulvae did not always respond so favorably. The incorporation of 1 to 2.5% of hydrocortisone with the estrogen in these patients has offered a better therapeutic response for local application in some patients with atrophic vaginitis.

A word about the use of estrogen in cosmetics would be appropriate at this time. Startling claims have been made by various manufacturers concerning the induction of youthful effects by estrogens incorporated in facial creams. These advertisements grossly exaggerate the therapeutic efficacy of their products, since the amounts of estrogens which are incorporated are below the therapeutic measure. We believe that estrogens given systemically in effective doses will produce a beneficial effect on the skin by increasing the deposition of elastic tissue. However, we must also state that the amount of estrogens in the cosmetic creams available to date is low and present only in homeopathic concentration, so that an adequate therapeutic response could not be anticipated. If the amount of estrogens were increased, this would place such creams and lotions in therapeutically effective ranges, so that sale over the counter would be prohibited, according to our present laws and regulations. The anticipated therapeutic action of such creams indiscriminately used would be expected to induce vaginal bleeding and other undesirable effects of hyperestrogenization.

Conclusions

The above therapeutic approach to the management of the menopausal patient has been offered as a means of treating a condition that can be distressing to both the physician and the patient. Wise management by the physician will result in a very grateful patient. The use of placebo therapy in appropriate cases may achieve the same therapeutic response as an estrogen. Placebo therapy in such patients is not a dishonest procedure but a means of treating a patient according to the dictums of our profession. The possibilities of sedation, psychotherapy, or estrogens and androgens furnish the physician with multiple modes of therapy for a complex problem and may induce relief in women who ordinarily would have to suffer through a rather unpleasant and possibly dangerous period of their lives. There is no need for these patients to suffer and say that they can bear their symptoms. Appropriately instituted therapy will create a happier patient and a better psychological clinical picture.

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PROLONGED ESTROGEN THERAPY IN POSTMENOPAUSAL WOMEN

Stanley Wallach, M.D.
and
Philip H. Henneman, M.D., Boston

The fact that estrogens have now been in therapeutic use for more than 25 years made it possible to examine the evidence for their safety and effectiveness in a study of 292 postmenopausal women. The mean duration of estrogen therapy in this group was 5.1 years per patient. The estrogens most used since 1945 have been diethylstilbestrol and conjugated equine estrogens, and the latter have been tolerated without side-effects by almost all patients. Among the commoner symptoms of the menopause, hot flashes were completely relieved in 93 of 94 patients. Postmenopausal osteoporosis was treated by prolonged estrogen therapy in 119 patients, 103 of whom had suffered collapse of vertebrae; either complete or significant relief from pain occurred in 90%. Evidence that estrogen therapy is prophylactic against postmenopausal osteoporosis was obtained in a group of 27 women. A study of the incidence of tumors among the 292 patients yielded no justification for the fear that mammary and cervical carcinoma may result from this therapy.

Cessation of ovarian function during middle life is a physiological event. However, lack of estrogen has been implicated as a major factor in the production of (1) the menopausal syndrome, consisting of hot flashes, fatigue, insomnia, and emotional lability; (2) postmenopausal osteoporosis[1]; and (3) the elevated beta:alpha-lipoprotein ratios[2] of postmenopausal women. It is generally recognized that estrogen administration induces positive balances of nitrogen, calcium, and phosphorus in women with postmenopausal osteoporosis[3] and corrects the postmenopausal serum lipid abnormality.[2] The present study represents a retrospective assessment of the efficacy and complications of prolonged estrogen therapy of the menopausal syndrome and postmenopausal osteoporosis.

Methods

The records of women treated with estrogens during the past 25 years were reviewed. Premenopausal women, patients who had never menstruated spontaneously, patients with acromegaly, and those with endocrine disorders associated with gonadotropin excretion of less than menopausal levels

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From the Department of Medicine of the Massachusetts General Hospital and the Harvard Medical School. Dr. Wallach is now at the Radio-isotope Laboratory, U. S. Naval Hospital, Chelsea, Mass. Dr. Henneman is now at Seton Hall College of Medicine, Jersey City, N. J.

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were excluded. Finally, the records of 292 postmenopausal women who received estrogen therapy for more than 12 months were studied in regard to (1) the modes, results, and side-effects of therapy; (2) the efficacy of estrogen therapy in the menopausal syndrome; (3) the effect of prolonged therapy on the incidence and course of postmenopausal osteoporosis; and (4) the incidence of breast and genital carcinoma during prolonged estrogen therapy. This group of women ranged in age from 15 to 83 years (mean age 51 years) and received treatment for a total of 1,480 years (mean 5.1 years of estrogen therapy per patient). Fifty-eight women had a spontaneous or artificial menopause before the age of 35. In 94 patients partial or total removal of the internal genitalia had been performed prior to therapy.

Modes of Therapy.—Prior to 1945 orally and intramuscularly given preparations of estradiol esters, estradiol pellets implanted subcutaneously, and long-acting parenterally given preparations of estrone and methylstilbestrol were most frequently used. The estradiol preparations were administered twice or three times per week with occasional medication-free intervals. The pellet and depot preparations provided continuous estrogenic stimulation. After 1945 these preparations were gradually replaced by orally given diethylstilbestrol, 1 to 3 mg. daily, or conjugated equine estrogens (Premarin), 1.25 to 5 mg. daily, administered cyclically in courses of 21 to 35 days with intervals of 7 to 10 days between courses. In women who had undergone hysterectomy the courses were 90 days in duration with intervals of 14 days between courses. In addition to being given estrogen replacement therapy 16 women were given the progestational agent anhydrohydroxyprogesterone (ethinyl testosterone), in doses of 50 mg. daily for the last five days of each course of estrogen. Fifty-one patients received methyltestosterone, 2.5 to 10 mg. sublingually daily, in addition to estrogen replacement therapy.

Patients were seen at four-week to six-week intervals during the initial period of therapy and two to four times per year after the establishment of satisfactory regimens. The patients' heights and weights were recorded at each visit, and all patients were asked to keep records of menses. Pelvic, breast, and vaginal cytological examinations were performed every 6 to 24 months. Roentgenograms of the spine and pelvis were obtained at one-year to five-year intervals.

Side-effects of Therapy.—Irregular and occasionally excessive uterine bleeding was common in women treated with preparations providing continuous estrogenic stimulation. Among the women treated after 1945 with orally given estrogens regular menses after estrogen withdrawal were induced in 90%. In 5% of patients irregular or excessive menstrual bleeding occurred, which was usually corrected by the addition of progestational agents. In the remaining 5% of patients the menses became scant or ceased after a few courses of estrogen replacement, and progestational agents were usually ineffective in reinstituting menses. This phenomenon occurred most frequently in elderly patients and in patients receiving combined estrogen-androgen therapy. Menstrual irregularity of sufficient severity to require curettage or hysterectomy did not occur in patients given cyclic oral estrogen therapy.

Nausea occurred in 20% of patients given diethylstilbestrol. Conjugated equine estrogens were tolerated by almost all patients and were substituted for diethylstilbestrol in patients intolerant to it. Blood dyscrasias, jaundice, or other manifestations of drug toxicity were not observed with either preparation. Excessive sodium and water retention occurred in 4% of patients, all of whom had preexistent cardiac disease. A diuretic regimen permitted continuation of estrogen therapy in the majority of patients with this complication. Urinary stress incontinence developed in 1% of the group and required cessation of therapy. Reactivation of endometriosis and of migraine headache occurred in one patient each. Nocturnal cramps were not observed.

Permanent discontinuation of therapy because of menstrual irregularity or any of the above-mentioned side-effects was necessary in 5% of patients. A similar incidence of side-effects occurred in women treated less than one year.

Estrogen Therapy of the Menopausal Syndrome

Ninety-four patients were treated primarily for severe symptoms of the menopausal syndrome. Many had been previously treated unsuccessfully with phenobarbital and other sedatives. In many instances the symptoms had been present for three or more years without spontaneous abatement. Complete remission of the hot flashes and significant or total alleviation of the related symptoms was achieved in 93 patients. Symptoms which existed prior to the menopause, including those of overt neuroses and psychoses, were not benefited by estrogen therapy.

Fifty-four women with onset of menopause prior to age 35 were given estrogen replacement therapy not only for the severe menopausal syndrome observed in this group but also prophylactically for postmenopausal osteoporosis. The effect of estrogen on the menopausal syndrome in this group and in women treated less than one year was identical with that observed above.

Estrogen Therapy of Postmenopausal Osteoporosis

Postmenopausal osteoporosis may be defined as a generalized loss of bone mass, affecting the spine most severely, which occurs in a small percentage of women after the menopause. The loss of bone mass is probably related to diminished estrogen secretion and decreased osteoblastic activity. Bone histology[1] is little altered; there is simply less bone. As total bone mass diminishes, bone resorption is decreased proportionately. Eventually, the rate of bone resorption approaches the postmenopausal rate of bone formation and little further loss of bone mass occurs. However, vertebral and other fractures continue to occur and the process may be accelerated by the decreased activity imposed by bone pain and by increasing age.

In affected women demineralization may appear as soon as two years and vertebral compression as soon as six years after the menopause. In patients with concomitant hyperthyroidism these changes may appear earlier. Fractures of the neck of the femur and humerus, of the wrist, and of the ribs after mild trauma are particularly common in women with postmenopausal osteoporosis. Serious neurological defects after vertebral fractures are rare.

In the present series 119 patients received prolonged estrogen therapy for postmenopausal osteoporosis. Serum calcium and phosphorus levels were normal in all patients. Transient increases in the serum alkaline phosphatase level were sometimes observed after fractures. Increased urinary excretion of calcium occurred in only a small number of patients. Collapsed vertebral bodies occurred in 103 patients. Postmenopausal etiology for the osteoporosis was considered presumptive in only 18 patients of this group because of antecedent immobilization secondary to trauma, arthritis, or neuromuscular disorder. Forty-two patients received small doses of methyltestosterone in addition to estrogen, without evidence of a superior therapeutic result. Surgical or radiologic castration or spontaneous menopause before the age of 35 years did not predispose to an earlier or more severe osteoporosis relative to the time of menopause.

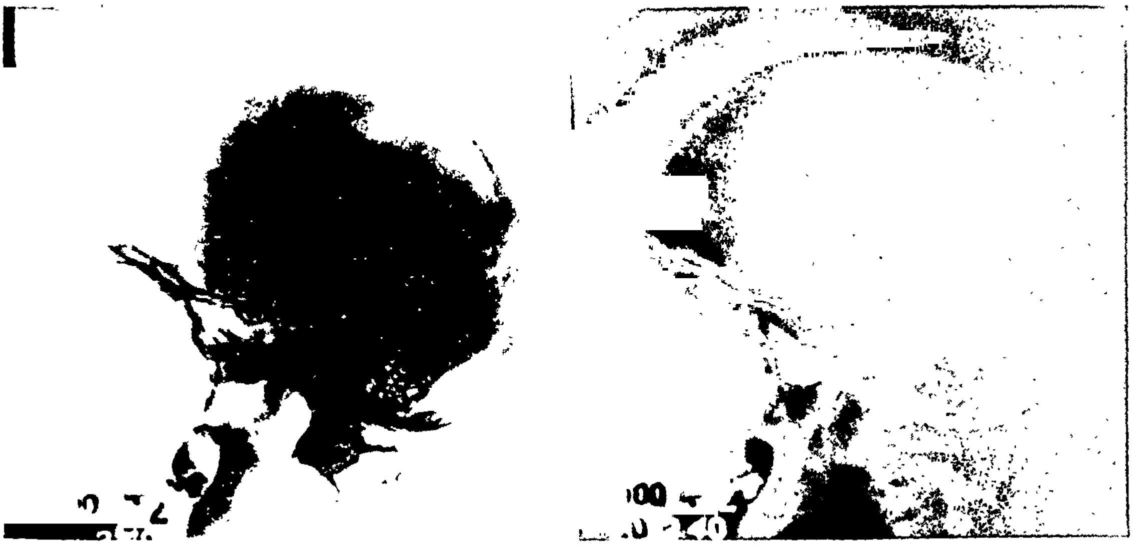

Fig. 1.—Roentgenograms of skull of patient, obtained on same day, showing variation in radiodensity due to radiologic technique alone. Roentgenographic appearance of skull is not abnormal in patients with osteoporosis.

The criteria chosen for evaluation of the results of estrogen therapy of postmenopausal osteoporosis were persistence of chronic back pain, loss of height, and roentgenographic progression of vertebral compression. Radiologic observation of density of the spine was found to be an unreliable parameter of changes in degree of osteoporosis, since marked differences in radiodensity occurred, due solely to variations in radiologic technique (fig. 1).[4] Height loss was adopted as a criterion because of a positive correlation between this parameter and roentgenologic evidence of vertebral compression. Among the 292 postmenopausal women under study premenopausal and postmenopausal heights were recorded for 94 patients previously determined to be free of lordosis, lower extremity fractures, degenerated intervertebral disks, or kyphosis of arthritic or neuromuscular origin. In 41 women no significant postmenopausal height loss occurred, whereas in 53 patients losses between 0.5 and 6 in. (1.25 and 15 cm.) occurred. Roentgenograms of the spine were available in 33 women who had no height loss and revealed vertebral demineralization in 4 but no instances of significant vertebral compression and no roentgenographic abnormality in 29. Among the 40 patients with height loss in whom roentgenograms were available decreased radiodensity alone was present in 8, and vertebral compression was evident in 30. In only two patients of the latter group were the spines roentgenographically normal.

Chronic back pain was the most common presenting symptom in the patients with osteoporosis. Complete relief or significant improvement of pain occurred in 90% of the patients treated with estrogen. Diminution in pain was usually reported within two months of initiating therapy, and progressive decrease in pain and increase in mobility were reported during the succeeding 6 to 10 months. In some patients this favorable course was punctuated by brief episodes of acute pain.

The effect of therapy on height loss and vertebral compression could be evaluated in 22 women with osteoporosis who received therapy for four or more years (fig. 2). These women had lost 1 to 5 in. in height prior to therapy and had compression of one or more vertebrae. Height loss ceased immediately after the initiation of estrogen therapy in 10 patients and within two years of initiating therapy in an additional 6 patients. One patient stopped losing height after three years of therapy. Five patients continued losing height, but, in three such instances, the total loss was 0.5 in. In two patients the height loss was apparently unaffected by estrogen therapy. Serial roentgenograms confirmed the height data in every patient. In no patient was there an unequivocal increase in radiodensity after therapy. Figure 2 also summarizes the results of estrogen therapy in 27 postmenopausal women without prior osteoporosis. During 4 to 25 years of estrogen therapy no significant back pain, height loss, or vertebral compression occurred.

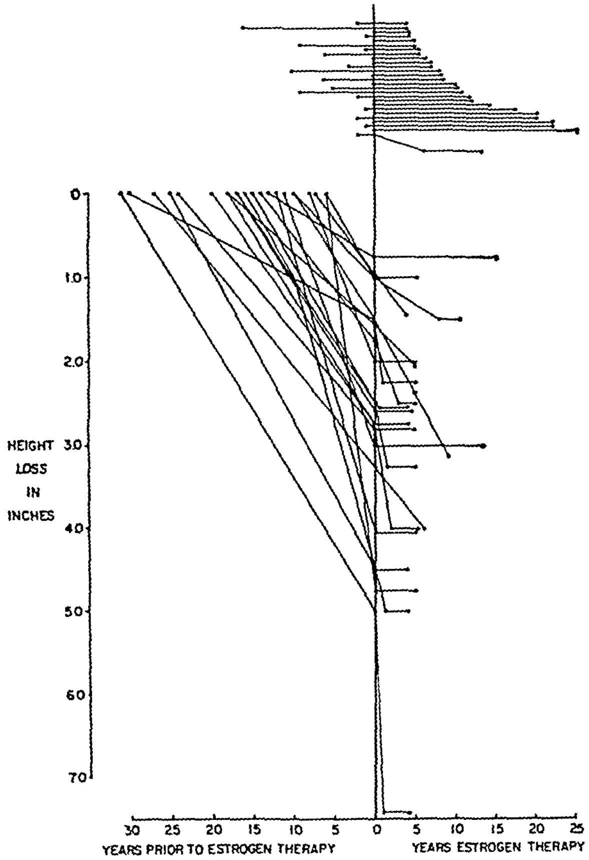

Fig. 2.—Height loss in postmenopausal women before and after estrogen therapy. Upper dots represent 27 women treated prior to development of osteoporosis, lower dots 22 women with osteoporosis at beginning of treatment. In 16 women with osteoporosis height loss ceased within two years of initiating therapy.

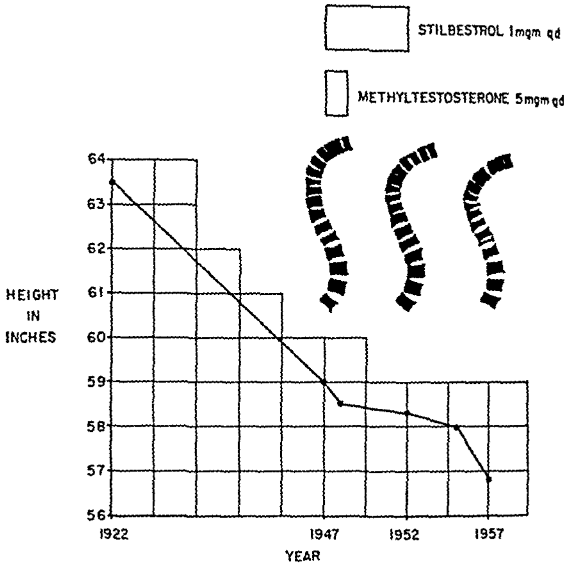

Fig. 3.—Summary of height and roentgenographic findings in 69-year-old woman with postmenopausal osteoporosis. Patient received estrogen therapy from 1947 to 1952. Height loss and vertebral compression resumed after discontinuation of therapy.

Figure 3 summarizes the height and roentgenographic findings in a particularly illustrative patient. This 69-year-old woman first developed back pain 24 years after a spontaneous menopause. Examination revealed marked kyphosis, compensated rheumatic heart disease, and a postmenopausal height loss of 4.5 in. (11.4 cm.). There was increased radiolucency of the thoracic and lumbar vertebrae, with compression of many vertebrae. Results of laboratory studies were normal. The patient was given diethylstilbestrol in doses of 1 mg. daily and methyltestosterone, 5 mg. daily, with a seven-day estrogen abstention period every fifth week. Regular withdrawal bleeding ensued. After three months of therapy back pain was improved and after 12 months completely absent. Height loss ceased after one year and androgen therapy was discontinued. During the third year of estrogen therapy peripheral edema developed, and the patient was treated with digitalis and diuretics. Estrogen therapy was finally discontinued after five years because of progressively severe edema. The patient was observed at intervals during the next five years. The edema regressed but did not disappear. Four episodes of acute back pain occurred in these five years, but chronic back pain did not recur. Despite these relatively mild symptoms a further height loss of 1.5 in. (3.7 cm.) and roentgenographic evidence of further vertebral compression occurred.

Occurrence of Breast and Genital Cancer

Primary carcinoma of the breast was not detected in any patient during estrogen therapy. Five women had been subjected to radical mastectomy for mammary cancer prior to therapy. One patient, whose original neoplasm had appeared 15 years after the menopause, developed a recurrent mammary carcinoma after six years of combined estrogen-progesterone therapy. In four patients the mammary carcinoma had developed shortly before the menopause. These four patients completed one to five years of estrogen therapy without incident.

Seven patients developed genital cancer during estrogen therapy (see table). Cervical carcinoma in situ developed in one patient after two years of cyclic diethylstilbestrol therapy. Overt carcinoma of the cervix did not occur in any patient. Two women developed ovarian cystadenocarcinomas. One of these patients had received oral therapy with a stilbestrol analog for two years with regular abstention periods, but the other had received five years of therapy with depot and pellet preparations of stilbestrol analogs.

Summary of Clinical Features of Seven Patients with Genital Carcinoma

Age, Yr.	Site of Cancer	Estrogen Therapy		Outcome
		Years	Type	
58	Cervix	2	Oral, cyclic	No recurrence 3 yr. later
53	Endometrium	2½	Oral, cyclic	No follow-up
48	Endometrium	6	Parenteral, depot	No recurrence 14 yr. later
68	Endometrium	8	Parenteral, depot	No follow-up
57	Endometrium	15	Parenteral, depot	No recurrence 1 yr. later
54	Ovary*	5	Parenteral, depot	No recurrence 11 yr. later
43	Ovary*	2	Oral, cyclic	Died of metastases 5 yr. later

* Cystadenocarcinoma.

Four patients developed adenocarcinoma of the endometrium. Three of these patients had received various combinations of parenteral, depot, and pellet preparations for 6 to 15 years before the neoplasm was detected. One patient developed an endometrial cancer after two years of cyclic oral diethystilbestrol therapy.

All six ovarian and endometrial carcinomas appeared prior to 1948. Only one genital cancer, a cervical carcinoma in situ, was detected in the last 10 years covered by this study, despite increased use of cervical cytological techniques. There were no breast or genital carcinomas in the patients treated less than one year.

Comment

The efficacy of estrogen replacement in treating the menopausal syndrome is well recognized, and its uniformly beneficial result contrasts with the commonly unsuccessful use of sedatives and other nonspecific measures. In postmenopausal osteoporosis the present report of a beneficial effect of estrogen on back pain, loss of height, and roentgenographic changes extend previous studies which demonstrated a favorable effect of estrogen on nitrogen, calcium, and phosphorus balance.[3] The small positive balances induced by estrogen in these studies may offer partial explanation for the failure to observe increased radiodensity after therapy and the interval between the initiation of therapy and the cessation of further vertebral compression in some patients. The cessation of further vertebral collapse in patients receiving estrogen therapy does not appear to be fortuitous in view of the uniformity with which the response is obtained, the severe and continuous vertebral compression observed in patients with idiopathic osteoporosis not amenable to estrogen therapy,[3] and the resumption of vertebral compression in patients with postmenopausal osteoporosis, if estrogen therapy is discontinued. The failure to develop osteoporosis in the 27 postmenopausal women in whom estrogen therapy was begun prior to the development of osteoporosis suggests that estrogen therapy is an effective prophylaxis for postmenopausal osteoporosis.

Serious side-effects of prolonged estrogen administration are infrequent and seldom necessitate discontinuation of therapy. The fear that breast and cervical carcinoma may result from this therapy appears to be unfounded. However, the incidence of endometrial carcinoma in this group of patients is many times the normal incidence.[7] The occurrence of four cases during the first 15 years and none during the last 10 years covered by this study is possibly the result of the regular desquamation of stimulated endometrium that occurs with cyclic estrogen therapy. Continuous estrogen secretion has been implicated in the increased incidence of endometrial carcinoma in patients with estrogen-secreting tumors.[8] The appearance of two cases of ovarian cystadenocarcinoma during the first 15 years of this study also exceeds the expected incidence.[7] The association may be fortuitous in view of the absence of other reports of this type of cancer in estrogen-treated women. Estrogen has no known stimulating effect on the ovary.

Summary and Conclusions

A 25-year retrospective study of the results of prolonged estrogen therapy in 292 postmenopausal women showed that serious side-effects were infrequent and necessitated discontinuation of therapy in only 5% of patients. Excellent results were obtained in the treatment of the menopausal syndrome and in postmenopausal osteoporosis. One case of

uterine cervical carcinoma and none of breast cancer occurred during prolonged estrogen therapy. Four cases of endometrial cancer and two of ovarian cystadenocarcinoma developed during the first 15 years of the study, but none were detected during the last 10 years of the study. This sharp decline in the incidence of genital carcinoma was related in time to a change from continuous to intermittent estrogen therapy. It is concluded that prolonged, cyclic, oral estrogen therapy combined with periodic pelvic and vaginal cytological examinations is a safe and effective therapy for postmenopausal women with disabling menopausal symptoms or postmenopausal osteoporosis. Its use in women with premature menopause is also recommended.

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Patient data used in this study were supplied by Drs. Fuller Albright, A. P. Forbes, E. C. Reifenstein Jr., F. C. Bartter, and P. H. Benedict.

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USE OF TRANQUILIZERS IN DERMATOLOGY

Wayne Wright, M.D., Hayward, Calif.

Nine tranquilizing medicaments were compared clinically with respect to their usefulness in treatment of patients with dermatological disorders. To be included in the series the patients had to be treated for not less than four months and were examined by the physician not less than 12 times. Of the 740 patients considered, 180 were dropped from the therapeutic study because of side-reactions but were considered in the study of complications. The blind method of drug selection was utilized for 420 patients. As a specific modality in the therapy of dermatoses it appeared that tranquilizing drugs had little to offer. The only possible exception was hydroxyzine hydrochloride for patients with nummular eczema. As adjunctive therapy phrenotropic drugs aid in three different situations: when pruritus is severe, when patients have difficulty in sleeping, and when steroid dosage is being reduced.

The fields of dermatology and psychiatry are thought by many to be closely related. Most psychiatrists and many dermatologists feel that several dermatoses are of psychogenic origin; prominent among the dermatoses most often described as being produced by psychogenic stimuli are psoriasis, lichen planus, pruritus ani and vulvae, atopic dermatitis, chronic urticaria, nummular eczema, and localized neurodermatitis.[1] It is logical that tranquilizing drugs would be used in the treatment of patients with skin disease, and in April, 1955, when Selling[2] reported that meprobamate cleared skin eruptions of psychosomatic origin, I decided to launch a controlled study of phrenotropic drugs in the therapy of patients with dermatoses. The main categories and subgroups of tranquilizing drugs used in the study are listed in table 1.

As shown in table 2, these drugs can be divided into two classes on the basis of their pharmacological actions, those that exert a suppressive effect on

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Assistant Clinical Professor of Dermatology, Department of Medicine, University of California School of Medicine, San Francisco.

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the autonomic nervous system (they act against or antagonize acetylcholine, histamine, and serotonin), and those that are central nervous system relaxants.

Materials and Methods

The sources of clinical cases were the outpatient and inpatient services of Travis Air Force Hospital in Fairfield, Calif., the psychiatric practice of Dr. Jean S. Wright, and the dermatological practices of Dr. Max Krause and myself. The study reported in this paper was undertaken on May 1, 1955, and terminated on April 1, 1959.

The patients had to be seen once or twice weekly for a period of two months and then at least twice monthly for two more months to be counted in this report. A total of 740 patients met this requirement. Because of side-reactions, results in 180 patients were dropped from the therapeutic data, but they were counted in the section on complications. Diagnosis and number of patients were as follows: psoriasis, 100 patients; pruritus ani and vulvae, 100 patients; lichen planus, 75 patients; atopic dermatitis, 150 patients; chronic urticaria, 100 patients; localized neurodermatitis, 140 patients; and nummular eczema, 75 patients.

Table 1.—*Classifications and Generic Names of Tranquilizing Drugs Used in Treatment of Patients with Dermatoses*

- Rauwolfia alkaloids
  - Reserpine
  - Rauwolfia
- Phenothiazine derivatives
  - Chlorpromazine hydrochloride
  - Prochlorperazine
  - Perphenazine
  - Trimeprazine
- Substituted propanediol
  - Meprobamate
- Diphenylmethane
  - Hydroxyzine hydrochloride
- Amides
  - Oxanamide

A blind study was done on 75% of the patients, with another physician selecting the drug and dose to be used. The one doing the follow-up on the case did not know which drug or drugs the patient was receiving or had received. Results were evaluated by the objective change in the skin condition and the patient's subjective signs of improvement in such symptoms as itching.

For a three-week period all patients were on therapy consisting only of administration of a tranquilizing drug. Topical and injected medicaments were withheld. It was deemed unfair to the patient to use only these orally given preparations if no subjective or objective improvement was noted in 21 days, but it is realized that three weeks may not be sufficient time for the tranquilizing drugs to prove or disprove their value.

The following drugs were alternated in all patients and, when possible, a three-week continuous regimen was maintained, with the dosage being regulated by a physician: rauwolfia, meprobamate, prochlorperazine, perphenazine, hydroxyzine hydrochloride, trimeprazine, and oxanamide. Neither excessive nor minimal amounts were used of any of the drugs.

Table 2.—*Pharmacological Actions of Tranquilizing Drugs*

Action	Drug
Group A: Those which affect autonomic nervous system	
Produce sleep pattern in electro-encephalogram, but not necessarily sleep	Reserpine Chlorpromazine hydrochloride
Block conditioned reflexes	Prochlorperazine
Prolong barbiturate anesthesia	Perphenazine
Lower electroconvulsive threshold	Hydroxyzine hydrochloride Oxanamide
Group B: Those which affect central nervous system	
Do not produce sleep pattern in electroencephalogram	Meprobamates
Have relaxant effect on spastic muscles	
Do not affect conditioned reflexes	
Increase convulsive threshold	

Results of treatment with orally given tranquilizing drugs alone are shown in table 3. It is seen that nummular eczema was the only condition in which significant improvement was noted, when administration of tranquilizing drugs was the only therapy. It is most interesting that, of the 37 patients with nummular eczema who improved, 30 were taking hydroxyzine hydrochloride in a dosage of 10 mg. three times daily. Of the remaining seven patients four were taking perphenazine, 4 mg. three times daily, and three were taking trimeprazine, one tablet three times daily. As yet, no reason is known why hydroxyzine hydrochloride was so effective in this clinical condition.

Table 3.—*Results of Treatment of Patients with Dermatoses with Tranquilizers Alone*

Diagnosis	No. of Patients	Result		
		Improved	No Change	Worse
Psoriasis	100	12	74	14
Pruritus ani and vulvae	100	16	72	12
Lichen planus	75	4	49	22
Atopic dermatitis	150	28	97	25
Urticaria	100	4	64	32
Localized neurodermatitis	140	18	91	31
Nummular eczema	75	37	29	9

The next approach in determining the value of tranquilizing therapy was to try to obtain the best possible clinical improvement in patients with accepted methods of therapy and then to add phrenotropic drugs to see if further improvement could be elicited. X-ray therapy was eliminated as a method in this phase. Treatment with steroids was used when not contraindicated. The results are shown in table 4. It is interesting to note that here again those patients treated with hydroxyzine hydrochloride showed an impressive improvement in the condition known as nummular eczema.

Complications

For the purpose of this paper the complications can be classified as dermatological and nondermatological. It also might be appropriate to further divide these into minor and serious reactions to the tranquilizing drugs. The minor nondermatological side-effects of the drugs used were blurred vision, nasal congestion, dryness of the mouth, changes in pulse rate, constipation, lactation in nonpregnant women, changes in menstrual cycle, urinary frequency, polyphagia, muscle spasm in the neck and shoulders, and significant rise in body temperature. No attempt was made to determine the percentage incidence of each type of reaction.

Among the more serious side-reactions of a nondermatological nature were convulsions, agranulocytosis, and sudden hypotension with syncope.

Table 4.—*Results of Treatment of Dermatoses with Usual Methods Plus Tranquilizers*

		Result			
		Improvement			
Diagnosis	No. of Patients	Subjective	Objective	No Change	Worse
Psoriasis	100	7	2	80	11
Pruritus ani and vulvae.	100	18	4	71	7
Lichen planus	75	4	0	60	11
Atopic dermatitis	150	24	8	104	14
Urticaria	100	3	3	77	17
Localized neurodermatitis	110	9	2	121	8
Nummular eczema	75	34	31	3	7

Convulsions.—Three patients in the study had convulsive reactions after a few days of therapy. Two were young men and the other a 48-year-old woman. All were taking 24 mg. of perphenazine daily in three divided doses. The woman had her first convulsion on the eighth day of the drug schedule. She later had a similar episode when hydroxyzine hydrochloride, 10 mg. three times a day, was given. Her convulsions after administration of hydroxyzine hydrochloride started on the fifth day of therapy.

One male patient, aged 19, had his first seizure on the fourth day of perphenazine administration, on a dosage of 24 mg. daily. The second male, aged 22, developed convulsions on the sixth day of perphenazine administration, with the same dosage. Both young men tolerated treatment with hydroxyzine hydrochloride, 10 mg. three times daily; prochlorperazine, 5 mg. three times daily; and meprobamates, without further convulsions.

Electroencephalography was done and the tracings of all three patients showed epileptiform patterns. None of the three admitted ever having convulsions before. It is well established that the convulsive threshold is lowered by the phenothiazines. Therefore, it follows that a careful history with regard to epilepsy should be taken before phenothiazines are prescribed by any physician.

Agranulocytosis.—A 54-year-old woman with lichen planus was given trimeprazine tablets, one four times daily, because of excessive pruritus. No other oral or radiation therapy had been administered to her in the previous 16 months. On the 11th day of treatment she became listless and developed a few small mouth ulcerations. Administration of the drug was stopped, and a white blood cell count showed 1,200 per cubic millimeter, which fell to 800 in three more days. She was treated with transfusions, antibiotics, and then steroids. Her white blood cell count did not return to a level of 4,000 per cubic millimeter until 42 days after administration of the drug had been stopped. No white blood cell count was done prior to administration of trimeprazine; however, there had been no reason to believe that it had been depressed.

White blood cell counts were then done on all patients being given phenothiazine therapy at two-week intervals after this experience. No other severe depression of white blood cells was seen. In six patients the white blood cell count fell to 3,000 during therapy with trimeprazine. However, administration of the drug was not stopped and the white blood cell count did not decrease further. These patients were checked every other day with a hemogram. In two of them the white blood cell count returned to about 6,200 while they were still receiving the drug.

No depression of white blood cells was seen in any of the patients taking phenothiazine derivatives other than trimeprazine. Fatal agranulocytosis after treatment with chlorpromazine has been reported by Tasker.[3]

Sudden Hypotension with Syncope.—Sudden hypotension with syncope was seen in three patients; all three were receiving meprobamates, and all three developed syncope within one week of taking the drug.

The first patient seen with this phenomenon of sudden onset of syncope was a 34-year-old woman with psoriasis. She reported that about 15 minutes after taking her "pill" she developed numbness and tingling of both upper and lower extremities and then fainted. She was alone at the time but estimated that she was unconscious for about 30 minutes. Examination of the drug schedule showed her to have been taking meprobamate, 400 mg. three times a day. It was on the fifth day of therapy that she had this episode.

A complete physical examination was within normal limits, except for the extensive psoriasis. Her blood pressure was 132/66 mm. Hg. While in the outpatient clinic she was given a 400-mg. tablet of meprobamate, with her permission, after careful explanation of the possible drug reaction. Within four minutes she complained of numbness of the fingers. Her blood pressure was 88/40 mm. Hg, and she was given epinephrine, 0.01 cc. of 1-1,000 dilution subcutaneously. Her blood pressure continued to fall, finally reaching 40/20 mm. Hg, and she lost consciousness for a brief period, less than two minutes. Her blood pressure slowly returned to 110/44 mm. Hg in the next 20 minutes, while she was at bed rest. Her body temperature rose from 98.4 to 102.6 F (36.8 to 39.2 C) orally and remained elevated for 49 minutes. Two young men taking meprobamate both reported identical symptoms of numbness and loss of consciousness. The drug was not readministered to them. All three patients later received therapy with perphenazine, hydroxyzine hydrochloride, and oxanamide, without similar reactions. Similar experiences have been reported, by Stroud[4] and others, in patients taking meprobamates.

Dermatological Reactions from Tranquilizers

Proof that all reactions were caused by the drugs was furnished by withdrawal of the drug until the eruption disappeared and then further administration of the drug until the same response was elicited.

The following types of skin eruptions were seen: urticaria, erythematous macular eruption, purpura, erythema multiforme, stomatitis, and a papulosquamous eruption closely resembling pityriasis rosea.

Urticaria.—Tranquilizers produced chronic urticaria in 14 of the group of 740 patients studied. The drugs responsible were meprobamates (nine patients), trimeprazine (one patient), perphenazine (two patients), hydroxyzine hydrochloride (one patient), and oxanamide (one patient), with no urticaria seen in patients taking reserpine or prochlorperazine. From patients seen for urticaria, other than those included in this study, 16 more cases of proved urticaria due to meprobamate administration have been seen in the past four years. Urticaria of this type has been previously reported by Becker and co-workers.[5]

Erythematous Macular Eruptions.—An erythematous type of macular eruption can be generalized or localized. In a few cases the eruption remained localized even though administration of the drug was continued. Pruritus accompanied the eruption in most patients but not in all.

Of the 740 patients 19 developed this erythematous macular eruption. The drugs responsible were meprobamates (seven patients), perphenazine (two patients), trimeprazine (one patient), hydroxyzine hydrochloride (three patients), oxanamide (one patient), reserpine (one patient), and prochlorperazine (four patients).

From among patients seen because of erythematous macular eruption during the past four years, other than those included in this study, nine more cases have been determined as being caused by meprobamates and three by prochlorperazine.

This type of reaction due to administration of tranquilizing drugs has been reported by Friedman and Marmelzat,[6] Becker and co-workers,[5] and Kositchek.[7]

Purpura.—Purpura was seen in 4 patients from among 740 in the study group. All cases were caused by administration of meprobamates; all patients had normal hemograms. Three additional patients have been seen in the past four years with purpura proved to be caused by meprobamates. Purpura as a side-effect of therapy with tranquilizers has been previously reported by Gottlieb[8] and Carmel and Dannenberg.[9]

Erythema Multiforme.—Generalized erythema multiforme was seen in eight patients in this study. Two could be classified as presenting Stevens-Johnson syndrome and were very ill. The drug was not given to these patients again after they had recovered. Both patients had been well until the second week of meprobamate therapy, taking a dose of 400 mg. three times daily, when the eruption appeared. The number of cases of erythema multiforme and the drugs which caused them were as follows: meprobamates (six patients), trimeprazine (one patient), and hydroxyzine hydrochloride (one patient). There were no patients with erythema multiforme among those taking perphenazine, oxanamide, reserpine, or prochlorperazine. Erythema multiforme due to treatment with meprobamates has previously been reported by Carmel and Dannenberg.[10]

Stomatitis.—Persistent and painful stomatitis was seen in two patients taking meprobamates. The lesions receded about four days after cessation of administration of the drug and reappeared on the first day after readministration. No other symptoms developed, and so this is classified as a different reaction from the erythema multiforme reactions, with accompanying mouth lesions. These two patients were given all the other tranquilizing drugs used in this study without recurrence of the mouth lesions.

Pityriasis Rosea–like Papulosquamous Eruption.—A typical picture of pityriasis rosea was produced in 3 patients of the 740 in the study group. All three were taking meprobamate drugs. All took the rest of the drugs being studied without developing the eruption. No reference to or report of a similar eruption has been found in the literature.

All three patients developed a lesion resembling a herald patch and then had eruptions typical of a clinical case of pityriasis rosea in from two to three days after the appearance of the herald patch. On cessation of the drug treatment the lesions faded in from five to seven days, but they could be reproduced in 48 hours after repeat administration of meprobamate. No systemic symptoms other than minimal pruritus accompanied the eruption.

In the past four years two other cases of this pityriasis rosea–like syndrome have been seen and proved to be caused by treatment with meprobamates. This gives rise to the possibility that pityriasis rosea is a drug eruption rather than a virus disease, as many people believe. The etiology has never been satisfactorily proved.

Comment

It should be emphasized that this paper has to do only with the tranquilizing drugs and their relationship to dermatology. No attempt has been made to evaluate their usefulness in the treatment of patients with other disorders.

As a specific modality in the therapy of dermatoses it is apparent that tranquilizing drugs have little to offer. The only possible exception is the use of hydroxyzine hydrochloride in nummular eczema. Enough patients were markedly improved when receiving hydroxyzine hydrochloride only to conclude that it merits a trial in treatment of patients with this condition.

As adjunctive therapy, phrenotropic drugs are of some value. They aid principally in three different situations: when pruritus is severe; when patients have difficulty in sleeping or feel tense most of the time, or both; and when steroid dosage is being reduced. Tranquilizing drugs often allow this reduction in steroids to be accomplished more rapidly, especially in the treatment of patients with atopic dermatitis.

The choice of drugs in each of the three situations varied somewhat with the individual patient, and often they would have to try two or three different ones before a satisfactory response was obtained. It should be noted that results of administration of reserpine have been left out, since the side-reactions were so great and the value obtained so minimal that it was not considered a satisfactory drug in the treatment of dermatoses. The list of drugs follows, in order of preference.

Oxanamide was the drug which afforded the most decrease in the intensity of itching and still let the patient carry out his normal activities. Trimeprazine was second choice in this category, even though it has been marketed for its antipruritic effect. Overall results of treatment with this drug were disappointing. A new form of trimeprazine in a sustained-release capsule is under investigation at the time of writing and appears to be an improvement on the present tablet. Prochlorperazine, perphenazine, and hydroxyzine hydrochloride all gave some relief of itching, but side-effects such as drowsiness interfered with the patients' normal daily routine. Meprobamate was considered a poor drug for relief of pruritus. Some patients even complained of increased itching.

For the dermatological patient who had difficulty in sleeping prochlorperazine, hydroxyzine hydrochloride, and perphenazine were about equally good, since they all produced drowsiness. Oxanamide and meprobamate were definite aids but less useful than the first three named. It was found that the dosage had to be slowly but continually increased over the period of treatment to retain the desired effect.

In patients receiving steroids in whom reduction in dosage was being attempted, oxanamide again proved to be the preferred drug. Prochlorperazine is the next most desirable drug, with the meprobamates being of least value.

Summary

Tranquilizing drugs are of no great value in the treatment of patients with dermatological conditions. Nummular eczema was the only specific entity definitely benefited by phrenotropic drugs, and the preferred drug for treatment of patients with this condition was hydroxyzine hydrochloride. As adjunctive therapy tranquilizers help to relieve itching, to produce sleep, and to allow steroid dosage to be reduced. Many side-reactions from phrenotropic drugs, both dermatological and otherwise, were seen. A pityriasis rosea–like syndrome, which has not been previously reported, was produced in five patients. Oxanamide seems to be the preferred drug, mainly because fewer complications have been seen, and less, although some, drowsiness is produced with this than with the other tranquilizing drugs.

Considering the cost of treatment with the phrenotropic drugs and the results obtained in dermatological patients, I recommended a therapeutic trial with phenobarbital before use of tranquilizers in a case in which a so-called tranquilizing effect is needed.

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CARDIAC CATHETERIZATION FOR DIAGNOSIS

DECREASED NEED, INCREASED COMPLEXITY, AND GREATER EXPENSE

Max H. Weil, M.D., Ph.D., Los Angeles

Improved methods of detection, and the survival of patients who formerly died during infancy or before reaching reproductive age, may well reveal a much larger incidence of congenital heart disease.[1] However, the number of patients who require cardiac catheterization for definitive diagnosis will not increase. The very fact that 12 years' experience with the technique has increased the accuracy of clinical diagnosis accounts for the lessened frequency with which cardiac catheterizations are now done.[2] It is apparent that precise diagnosis in a majority of patients with congenital heart disease as well as patients with acquired heart disease may be achieved by purely clinical techniques.[3]

Diagnostic Approach

The detailed history, physical examination, x-ray studies, and electrocardiographic data are often sufficiently distinctive for definitive diagnosis. This is most vividly demonstrated by recent practice at the Mayo Clinic, where about 90% of pediatric patients with tetralogy of Fallot are referred for surgery on the basis of clinical diagnosis achieved without cardiac catheterization.[2] Only more complex lesions are referred for cardiac catheterization. Such complex diagnoses require elaborate techniques, which, in addition to pressure and oxygen content determinations, include the recording of indicator dilution curves, multiple simultaneous pressure measurements, and selective angiocardiography or cineangiography. It is therefore essential that diagnostic laboratories have sufficiently elaborate instrumentation, competent technical and nursing staff, and generous provision for physical work space in order to provide these services.

Expansion of Laboratory Facilities.—The expansion of facilities for cardiac catheterization is a natural outgrowth of acceptance of cardiac catheterization and the practical advances of cardiac surgery. However, the establishment and support of a large number of cardiovascular laboratories in the same geographical area requires serious consideration. The financial burden of development and maintenance of a proficient cardiac catheterization laboratory is such that the unit can hardly be self-sufficient. In addition to the need of costly physical space in a hospital area, the expense of special installation in a properly equipped laboratory may be in excess of $100,000. A summary of actual costs involved in the establishment of one such unit is presented in the table.

Expenditures for Improvement.—The remarkable developments in the past and those which continue to take place in cardiac catheterization and related techniques exact their price, for equipment requires replacement as major improvements and refinements are introduced. The fluoroscope is replaced by the image intensifier, and 2-per-second angiography is replaced by 12-per-second biplane angiography. For this reason, purchase of equipment becomes a continuing necessity if standards are to be maintained. It is estimated that the basic expenditure will be repeated at the end of five years.

Cost of Operation.—Successful conduct of the laboratory requires a competent medical staff on at least a half-time basis. In our laboratory, each procedure requires participation of a minimum of two physicians, a nurse, and three additional technically trained persons. In small children, the availability of a highly skilled anesthesiologist is a prerequisite if the patient's safety is to be assured and sufficient circulatory stability is to be obtained to allow for definitive measurements.[4]

If three cardiac catheterizations are done weekly, the cost of technical and nursing personnel for each procedure is about $130. This is exclusive of the fee for the cardiologist's services or for anesthesia. Expendable items such as catheters, x-ray film, radiopaque mediums, and recording paper add about $65 for each procedure. To assure smooth operation and a reasonable minimum of technical failures, we have found it necessary to provide for constant activity with a schedule of three catheterization procedures each week. For the safety of the patients, availability of cardiac resuscitation equipment, proximity to surgery, and the cooperation of a thoracic surgeon have been essential and reassuring. Interpretation of the crude data, calculations, and compilation of the report are done by a cardiologist. In the case of a typical right heart catheterization, this phase of the work requires as much as eight hours of one physician's time.

Complications and Risks.—Catheterization of the heart and great vessels is a major diagnostic undertaking which is not without danger. The risk of death for patients undergoing right heart catheterization in an established cardiac center is between 0.1 and 0.4%. In infants under one year of age, the mortality of cardiac catheterization is as high as 1.5%. Angiocardiography almost doubles the hazard of a fatal outcome and thoracic aortography has a mortality of about 1.0%.[5]

Short episodes of ventricular tachycardia frequently occur during routine catheterization of the right ventricle. These rarely lead to ventricular fibrillation. However, four instances of ventricular fibrillation were recently reported in a series of

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From the Department of Cardiology, Elsinore and George Machris Cardiac Hospital, City of Hope Medical Center, Duarte, California, and the Department of Medicine, University of Southern California, School of Medicine, Los Angeles.

more than 1,500 patients undergoing catheterization of the heart. Successful defibrillation was achieved in three of the patients, indicating the importance of good resuscitation maneuvers.[6] Other complications include pyrogenic reactions, acute congestive heart failure, thrombophlebitis or arteritis, and embolization. Knotting of the catheter occurs with surprising infrequency. Cardiac standstill or perforation of a major blood vessel or of the heart are rare occurrences indeed, but these require immediate surgical assistance. Patients who have shunting of blood from the right to the left heart present special dangers of embolization. Severe pulmonary stenosis or abnormality of tricuspid valve placement (Ebstein's anomaly) provide conditions in which judicious reserve rather than completeness of the catheterization study may be assurance against a fatal accident. A total of more than 100 catheterizations have been done in our new laboratory in the past year. Only one complication was experienced when a knot was tied in the cardiac catheter while it was lodged in the superior vena cava. The catheter was withdrawn to the right axillary vein, from which it was removed by venotomy.

Cost of Cardiac Catheterization Equipment[*]

Radiologic equipment and supplies		
Installation and cables	$ 8,636	
Roentgenographic and fluoroscopic unit	23,000	
Image amplifier	6,000	
Bi-plane angiocardiographic unit	20,000	
Generator	8,300	
Tube crane	3,207	
Angiocardiographic pressure injector	716	
Incidental radiology equipment	780	
		$ 70,639
Electrical installation		3,419
Recorders		
Electronics for medicine	10,000	
Brown recorders and connecting cables (2 units)	2,155	
Tape recorder	346	
Dictaphone recorder (model T.A. 5)	320	
		12,821
Oximetry and dye dilution equipment		6,797
Pressure transducers		2,533
Accessory instrumentation (cardiotachometer, ergometer, spirometer, etc)		1,611
Table accessories		683
Gasometry laboratory		3,148
Carpentry		695
Initial catheters, stopcock, and needle supplies		1,338
Incidentals		250
Total		$103,934

[*] Based on costs quoted during academic year 1957-1958.

When cardiac catheterization is required for definitive diagnosis and determination of operability, these hazards should rarely dissuade the physician from recommending the study. However, the risks should be minimized by the selection of an experienced team and the availability of ancillary services and facilities that assure maximum safety.

Comment

The very fact that the clinician looks to the laboratory for specific information to achieve a diagnosis he cannot make from clinical data alone requires a high level of confidence in the acquisition and translation of crude data into a definitive diagnosis. Economic and technical limitations leading to the establishment of laboratories that employ short-cuts and compromises thwart the very purpose for which cardiac catheterization procedures are employed. The clinician (and the patient) has a right to look to the laboratory for precise and complete data on the completion of a catheterization. Referral to a larger unit as a consequence of technical limitations hardly seems justified. The thesis that every cardiac clinic needs its own cardiac catheterization unit is hardly practical. Would it not be far better to pool professional and financial resources and thereby provide generous support of a centralized laboratory? Cardiac clinics throughout a geographical area, each of which has but a limited number of patients requiring detailed studies, would share the advantages provided by a laboratory which is more adequately staffed and equipped.

Summary

There is a decreased need for cardiac catheterization as a method of cardiac diagnosis. However, patients with complex lesions which defy clinical diagnosis need detailed studies which use increasingly elaborate techniques and costly facilities. Establishment of small units with formidable technical and economic limitations thwarts the purpose for which cardiac catheterization procedures are now done. Consideration should be given to development of centralized diagnostic laboratories serving several hospitals and clinics.

1500 E. Duarte Rd., Duarte, Calif.

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EVALUATION OF TRANQUILIZING DRUGS IN MEDICAL OUTPATIENTS

MEPROBAMATE, PROCHLORPERAZINE, AMOBARBITAL SODIUM, AND PLACEBO

Karl Rickels, M.D., Thomas W. Clark, M.D., James H. Ewing, M.D.
Walter C. Klingensmith, M.D., Harold M. Morris, M.D.
and
Charles D. Smock, Ph.D., Philadelphia

Fifty-one psychoneurotic outpatients participated in a study in which the effects of four drugs were compared. The main symptoms were anxiety, tension, and mild depression, in the absence of detectable organic disease. Complete data were obtained from 28 patients who took all four drugs in random order. The drugs were given each four times a day for two weeks in the following doses: amobarbital sodium, 30 mg.; meprobamate, 400 mg.; prochlorperazine, 5 mg.; and placebo. Precautions were taken to eliminate bias arising from personal interactions, from the order in which the drugs were taken, or from the fact that 23 patients dropped out before completing the study. The three active drugs and the placebo all influenced the patients significantly during the first two weeks, but thereafter only the three active drugs gave significantly better results. Therapy with meprobamate always produced the most marked change toward improvement and most often showed a significant difference between drug and placebo in the dosages used.

Tranquilizing agents are prescribed today at an ever-accelerating rate not only by psychiatrists but, to a much greater extent, by nonpsychiatric physicians. Many clinical studies report favorable results achieved with use of different tranquilizers in the treatment of patients suffering from tension and anxiety. But, while a number of studies have used a controlled methodology in the form of a blind or double-blind technique for the evaluation of results of treatment in psychotic inpatients, only a few well-controlled studies have been done on the nonpsychotic outpatient population.[1] Furthermore, most authors have focused their attention on the study of outpatients frequenting psychiatric clinics and not on the evaluation of patients seeking help from the nonpsychiatric physician.

A therapeutic approach, combining the effect of tranquilizers with the physician's understanding and helpful attitude, leads to improvement in many patients, at least symptomatically. Loss or decrease of symptoms often enables the patient to deal with his problems more efficiently and to build up or to reestablish more adequate defenses; often, by so doing, he is bolstered against further stress.

Purpose of Study

This double-blind, controlled study was instituted because of the great need to evaluate the new drugs used in the treatment of patients suffering from tension, anxiety, and mild depression. Its purposes are as follows: (1) to determine the therapeutic efficacy of two tranquilizers and one sedative and to compare them with placebo; (2) to learn more about methods of studying emotionally disturbed patients attending a medical outpatient clinic and to develop improved techniques for the evaluation of drug therapy; (3) to compare a number of clinical tests and methods of evaluation; (4) to seek to profile clinical drug effects, as well as to determine such gross changes as "improved" and "unimproved"; (5) to study the response to drug therapy of a population group similar to that which the nonpsychiatric physician treats in his office; and (6) to control and minimize the personal element of the doctor-patient relationship in order to approach the determination of pure drug effects.

Drugs Used.—Many clinical studies done on outpatients report favorable results obtained from treatment with meprobamate (Miltown or Equanil),[2] but the few controlled studies that have been published are evenly divided into favorable and unfavorable reports.[3] Prochlorperazine (Compazine) is an even newer drug than meprobamate and has been favorably reported in clinical reports.[4] However, no well-controlled study on its use with outpatients has yet been published. Amobarbital sodium has been known for decades to be effective in improving certain tension states. Recently, a double-blind study has shown that it produces a definite change in patients suffering from anxiety.[1d] Amobarbital sodium, rather than phenobarbital sodium, was chosen because of the lower incidence of depressive moods produced by the former drug. An inert placebo control was chosen because of the well-known and much-discussed therapeutic effects

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From the departments of psychiatry (Drs. Rickels, Ewing, Morris, and Smock) and medicine (Drs. Clark and Klingensmith). Dr. Smock is now at the Department of Psychology, Purdue University, Lafayette, Ind.

produced by an inert substance when given to a patient by a physician whose helpful attitude is obvious.

Subjects and Procedures

Population.—Fifty-one outpatients, selected from the medical outpatient clinic of the University of Pennsylvania, participated in this study. A heterogeneous group of psychoneurotic patients, carrying the diagnosis of psychoneurosis or character neurosis, was chosen. Although they had come to the clinic because of physical pain and tension no pathological lesions could be found. Their main symptoms were anxiety and tension, often partly symptomatized and also mild depression. Mild depression often accompanies anxiety and generally goes unnoticed by most physicians.[5] Excluded from this study were patients with severe depressions, all patients with physical, nonemotional illness, even if not related to their present symptoms, and all patients suffering from such psychosomatic disorders as ulcerative colitis, peptic ulcer, and asthma. No limits as to age, sex, and race were set, and the actual age range was 25 to 60 years.

Medications and Design.—Meprobamate, prochlorperazine, amobarbital sodium, and placebo were dispensed in identical capsules, and each patient was given a supply of one of these medicaments that would last a little over two weeks. He was instructed to return any unused capsules. This provided some control of how many capsules each patient took during a given interval.

Each patient was told to adhere rigidly to the schedule but was allowed to reduce his medication if he became too drowsy and if his sleepiness interfered with his daily functions. The patient took two capsules four times daily of the drug assigned to him for a two-week period, each capsule containing one of the following amounts: amobarbital sodium, 15 mg.; meprobamate, 200 mg.; prochlorperazine, 2.5 mg.; or placebo. Thus, the respective daily doses of patients not receiving placebo were amobarbital sodium, 120 mg.; meprobamate, 1,600 mg.; or prochlorperazine, 20 mg.

Each patient was placed on therapy with each of these four medicaments for two weeks, with use of a double-blind technique and according to a completely randomized design. It was felt that an effective drug should produce at least minimal improvement in the patient during this time.

None of the physicians participating in the study knew, at any time, which drug a particular patient was receiving, and the kind of side-reactions reported did not allow differentiation between drugs, since quite a few patients reported more side-reactions from therapy with the placebo than from that with any of the three active drugs.

Evaluative Procedures.—A variety of procedures, such as rating scales, a check list, and a clinical questionnaire, were used to determine the comparative efficacy of the three active drugs and the placebo.

Taylor Manifest Anxiety Scale and Saslow Screening Inventory: To demonstrate change occurring during the entire eight-week course of this study, irrespective of the order of drug administration, two well-established tests, the Taylor Manifest Anxiety Scale[6] and the Saslow Screening Inventory,[7] were given to each subject twice, once at the beginning and once at the conclusion of the study, although, usually, neither scale is used for measuring "change" in psychiatric status.

Four additional tests were given at the onset of this study and subsequently every two weeks, a total of five times.

Over-all Absolute Rating Scale (0–8): An over-all absolute rating scale represents an over-all rating of a patient's emotional status on a continuum from no symptoms (0) to most severe symptoms (8). The patient as well as the physician, independently of each other, marked an "X" at that point of the scale which they felt best represented the patient's present emotional status.

Over-all Relative Rating Scale (−3 to +3): An over-all relative rating scale of seven points indicates change of a patient's condition on a bipolar spectrum. Patient as well as physician scored independently of each other how the patient felt during the last three days in comparison to two weeks previously, at the time of his last evaluation. The patient could feel worse (−3, −2, −1), the same (0), or better (+1, +2, +3).

The reproducibility of both scales was very high. The two physicians who performed all interviews saw 14 patients together a total of 27 times and evaluated them independently. The interviewer was chosen at random. The absolute rating scale was evaluated 27 times and the relative scale 13 times. Neither interviewer differed more than one point on the former scale and, when seeing the patient for the second time after two weeks, the direction and degree of change was, in every evaluation, the same. Both interviewers agreed 100% in the 13 evaluations of the over-all relative rating scale.

Duke Check List: The Duke check list,[8] developed for patients with an educational level of 4 years or above and validated by researchers from Duke University, consists of 99 weighted items covering a variety of areas of nonpsychotic psychopathology and of 41 questions referring to physical symptoms.

Clinical Questionnaire: The clinical questionnaire consists of 45 questions covering several areas of psychopathology. These questions were set up to categorize symptomatology under the headings of anxiety, depression, obsessive-compulsive tendencies, phobia, irritability, and reported side-effects of the drugs used. This set of questions was developed from a 34-point scale used by Meath and associates.[1a] Each question was rated on a four-point scale, the higher score indicating greater distress.

To determine how accurate the ratings could be made, both physicians independently evaluated 14 patients a total of 27 times during the course of this study. They differed in only 1.6 out of a total of 45 questions and never differed by more than one point. This high degree of reliability was thought to allow subsequent rating by one physician only.

It should be stressed that the reliability established for repeated testing does not tell us whether the questionnaire as a whole is a reliable instrument in measuring a great variety of neurotic symptoms; it only tells us that the data found by two observers independently of each other were almost identical.

Table 1.–*Medicament Received by Twenty-three Patients Who Dropped Out During Drug Evaluation Study*

Patient Group	No.	Amobarbital Sodium	Meprobamate	Prochlorperazine	Placebo
Initial "drop-outs"	16	5	1	5	5
Late "drop-outs"	7	4	1	5	2

General Procedure.–All patients were first seen by a technician who administered all tests that the patient was to fill out himself, collected the returned bottles, and gave all patients their new supply of medicaments for the next two-week period in coded bottles, together with an information sheet.

Each patient was told that we had a new drug that might benefit him, that at the end of the trial he would be supplied with the medicine that had helped him most, and that the name of the drug would be made available to him and to his private physician.

Each patient was then seen by either of two physicians, (K. R. or T. W. C.), one a psychiatrist and the other an internist. The patient was asked all 45 questions of the questionnaire by the physician, each question being pursued, if necessary, to clarify a response. Questions usually arose only in regard to degree of symptom, and it was mutually decided to inquire into degree of severity by asking: "Is this . . . . symptom present just a little bit, quite a bit, or all the time?" To keep the therapeutic relationship between patient and doctor to a minimum, most patients were seen by both physicians during the course of the study.

Table 2.–*Patient Groups and Mean Test Score of Fifty-one Patients Before Therapy with Drugs*

No.	Patient Group	Absolute Over-all Rating-Scale (0-8) Mean	Absolute Over-all Rating-Scale (0-8) Range	Clinical Questionnaire Score Mean	Clinical Questionnaire Score Range
28	Study completed	4.5	3.0-7.5	37	10-66
16	Initial "drop-out"	4.2	1.5-7.5	28	11-64
7	Late "drop-out"	5.7	4.5-6.5	49	36-59

Results

Evaluation of Patient Participation.–Of 51 patients who participated in this evaluation, 28 completed the study by taking all four drugs in random order, and 16 failed to return after their first visit. Of seven patients who dropped out in the later stages of the study, one dropped out after four, three after three, and three after two visits. All of these seven patients expressed dissatisfaction with the help they had received. Table 1 relates failure to complete the experiment to type of medicament administered.

The initial over-all rating (by both patient and physician) and the questionnaire scores for the three different groups of patients before administration of the drugs are presented in table 2. The scores obtained before administration of the drugs from the group of patients who completed the study as well as those of the group who dropped out early differ significantly from the scores of the group who dropped out late ($p=0.02$, Whitney U test, two-tailed).

The data in table 2 seem to indicate that patients who completed the study and patients who dropped out early suffered from mild to moderately intense symptoms, while the patients who dropped out late, as a group, suffered from more severe symptoms, as indicated by the mean score. They dropped out only after having lost hope for improvement and having expressed this to the doctor.

Patients' Preferred Choice.–An analysis of our patients' drug preference indicated that they preferred meprobamate (table 3). This preference was elicited by asking all patients, after conclusion of the study and before breaking the double-blind design, "Which batch of medicine do you think helped you most?" They were asked to indicate first and second choice.

Table 3.–*Preferred Drug Choice of Twenty-eight Patients*

Drugs	Patient's Choice 1st	Patient's Choice 2nd*	Unused Medicament, % of Total Drug
Meprobamate	17	16	12
Prochlorperazine	7	10	16
Amobarbital sodium	3	7	18
Placebo	1	1	18

* Four patients made no second choice.

Over-all Improvement During Eight-Week Study Period.–Improvement of patients over the whole study period, irrespective of order of drug administration, was demonstrated by all test measures. This trend was also confirmed by our inspection of the Taylor and Saslow scales. Neither scale was analyzed statistically, however, since they were filled out by only 19 patients.

The degree of initial symptoms in our patient group did not influence the rate of individual improvement. This is demonstrated in table 4, which shows that patients with a high initial symptom score improved in roughly the same proportion as patients with a low initial symptom score, irrespective of order of drug administration.

Analyses of Drug Effects

Over-all Analysis of Clinical Questionnaires.–All four treatment conditions (amobarbital sodium, meprobamate, prochlorperazine, and placebo) brought about significant changes beyond the 5% level of confidence, as demonstrated by an analysis of the variance by means of total scores of the questionnaire and by testing the over-all effect of the four treatment conditions (above the order of drug administration and beyond the influence of time sequence). This over-all analysis permitted specific, detailed analysis, comparing each drug with every other for over-all as well as differential effects. Inspection of the data showed that, while the improvement rates of the three active drugs were divided among the four treatment periods, most of the improvement from treatment with placebo took place in patients receiving placebo as their first medicament.

Evaluation of Each Two-Week Period.—Since the analysis of variance showed that all four drugs improved the patients' condition significantly, it seemed of interest to graph the over-all drug effects against the four two-week periods.

If one plots the difference in scores of the total clinical questionnaire before and after drug evaluation, irrespective of which drug has been given before, one sees that all four drugs caused significant improvement during the first two weeks of study. During the following six weeks, however, the mean scores of the patients receiving placebo became negative while those of the patients given the three active drugs stayed positive (see figure).

TABLE 4.—*Total Questionnaire Rating of Symptoms Versus Improvement*

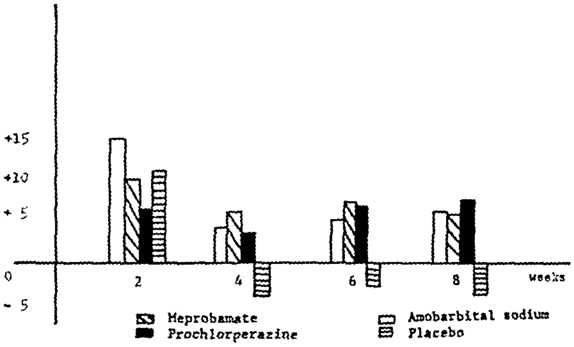
Patient Group	Before Study	After Study	Change, %
High symptom score	53	29	54.7
Low symptom score	20	11	55

Results of Absolute and Relative Over-all Rating Scales.—Four statistical comparisons were made; they are as follows:

Drug Effect Compared with Condition Prior to Treatment with Drug: Both rating scales correlated highly with each other. The physician in general showed a tendency to rate improvement on both tests somewhat more conservatively than the patient did. In several instances a physician was unable to evaluate the patient on the relative scale, because not he but the other physician had seen the patient two weeks before.

The T-test for correlated data showed that administration of all three active drugs, on both absolute and relative tests, resulted in significantly greater improvement than lack of treatment, while administration of placebo did not produce significant change. The p values (one-tailed T-test) for the results appearing in the relative scale filled out by the patients are as follows: meprobamate, $p=0.001$; prochlorperazine, $p=0.001$; amobarbital sodium, $p=0.02$; and placebo, $p=0.5$. Application of the nonparametric sign test to both scales showed significant improvement under amobarbital ($p=0.05$), prochlorperazine ($p=0.005$), and meprobamate ($p=0.001$). It has to be realized that the sign test measures only direction, not degree of change.

Drug Effect Versus Placebo Effect: Evaluation of drug versus placebo effect is shown in table 5, which presents a comparison of the efficacy of each of the three active agents with that of placebo (T-test for correlated data) on the basis of the data from the "over-all relative scale" which had been filled out by the patient himself. Patient and physician on the "relative over-all scale" showed almost 100% agreement. This can be explained by the fact that the physician's rating relied heavily on the patient's own statement about his improvement or lack of improvement. No significant difference in the efficacy of the three active drugs was found in either test.



Mean difference scores for four medicaments during four two-week periods (clinical questionnaire).

Result of Clinical Questionnaire: In our evaluation of the clinical questionnaire, we have utilized difference scores (e. g., the score after intake of drug A is equivalent to the score before intake of drug B). We feel that such an evaluation will give more reliable results than the use of total scores,[9] even if the "difference scores" might tend to deflate the value of a given drug. By making use of difference scores, we expect to show that use of agents which are not as good as the ones previously received brings no improvement or a change toward the worse.

Over-all Drug Effects Versus Placebo Effects: Table 6 gives the over-all efficacy of amobarbital sodium, meprobamate, and prochlorperazine in the treatment of our patients above the level of that produced by placebo, as measured by symptom scores of the clinical questionnaire.

TABLE 5.—*Over-all Improvement (Relative Scale) in Twenty-eight Patients*

Medicaments	T-Tests (One-Tailed)	Sign Tests (One-Tailed)
Amobarbital sodium vs placebo	$p=0.1$	$p=0.2$
Meprobamate vs. placebo	$p=0.01$	$p=0.01$
Prochlorperazine vs. placebo	$p=0.05$	$p=0.02$

Symptom Cluster and Item Analysis: In table 7 the three active drugs are compared with placebo by the same method as used above. An item of the 45-symptom clinical questionnaire was assigned to anyone of the five clusters of table 7, provided five of six psychiatrists who were not related to the study agreed in placing the item in one of these five categories. Actually, a sixth category, "obsessive-compulsive tendencies and phobia," was used, but none of the four drugs was found to have any influence whatever on this cluster.

TABLE 6.–*Improvement (Difference Scores of Clinical Questionnaire) in Twenty-eight Patients*

Drugs	p Values, One-Tailed T-Test
Amobarbital sodium vs. placebo	0.1
Meprobamate vs. placebo	0.05
Prochlorperazine vs. placebo	0.2

Table 7 shows that meprobamate was most effective in treatment of depression and irritability symptoms, was not effective at all in treatment of the gastrointestinal symptoms, and compared favorably with the other active drugs in treatment of symptoms of anxiety. Our finding that meprobamate significantly influences symptoms of irritability and depression confirms former clinical reports.[1c] Our patients, however, were not primarily depressed patients but suffered, as many anxious patients do, from certain depressive symptoms. Prochlorperazine was most effective in treatment of gastrointestinal symptoms.

The number of our patients who suffered predominantly from gastrointestinal symptoms was not large; hence, it is felt that even a p-value of 0.1 in this case seems to represent a higher level of confidence than it usually does. Amobarbital sodium was not at all effective in treatment of gastrointestinal symptoms but was effective in the treatment of the other three conditions rather evenly, even if not significantly. Our results confirm impressions of other authors, as well as the clinical experience of two of us (J. H. E. and K. R.), who noted improvement in ulcerative colitis and irritability of the colon after treatment with prochlorperazine.

More patients suffered from somatic side-reactions, mainly sleepiness during the day, when given amobarbital sodium than when treated with any of the other drugs. Prochlorperazine, in the dosage used, produced the fewest side-reactions, while patients given placebo often complained about side-reactions, mostly sleepiness.

Further inspection and evaluation of the questionnaire showed that certain single items seemed to be influenced differentially by some drugs, above the level of the differential cluster effects. Of these items insomnia, excessive sleepiness, and headache were examined further. The efficacy of each of the three active drugs was compared with that of the placebo. The results showed that some persons with headache benefited from therapy with prochlorperazine, others from meprobamate, and a few from amobarbital sodium. There was no significant difference between the effects of all three drugs, but it seems that prochlorperazine is more effective in treatment of the migraine or cerebral type of headache, while meprobamate is more effective in tension headaches. Further studies would have to confirm this finding. Insomnia was improved almost solely and consistently by therapy with meprobamate ($p=0.005$, T-test; $p=0.01$ sign test). This confirms other clinical reports.[1e] Administration of amobarbital sodium and prochlorperazine had no significant effect on this item.

Analysis of the item "excessive sleepiness during the day" revealed no significant difference between the three active drugs and placebo. Administration of amobarbital sodium produced more drowsiness than meprobamate but was far less effective in alleviating insomnia. This finding is in contrast with results reported by others[1d] who used even higher dosages of amobarbital sodium (100 mg. three times a day) than we did, without reporting side-reactions. Since these authors reported only over-all change we are not able to say what particular symptom change, if any, brought about decrease of the patient's anxiety. The "sleepiness" score for prochlorperazine was lower than for placebo, while it was higher for amobarbital sodium and meprobamate, that for amobarbital sodium being higher than that for meprobamate.

It was of interest to note that almost invariably patients with insomnia who improved when given meprobamate did not complain about excessive sleepiness during the day, while patients whose insomnia was not influenced by meprobamate did complain. In other words, there seems to exist an inverse relationship between improvement of sleep and the side-reaction "excessive sleepiness during the day." Seventy-five per cent of our patients suffered from varying degrees of constipation. All four experimental conditions influenced this symptom randomly and significantly.

Analysis of Duke Check List.–Since only 12 of the 28 patients who completed the study were able to fill out the Duke check list properly, this test was not submitted to statistical analysis. However, an inspection of the data obtained from the Duke check list showed that the direction of change corresponded highly with the direction and degree of change demonstrated by other test measures. This suggests that the Duke check list is a good

TABLE 7.–*Results of Cluster and Item Analysis (Clinical Questionnaire) in Twenty-eight Patients**

Drugs	Anxiety, 10 Questions	Depression, 12 Questions	Irritability, 5 Questions	Gastro-intestinal Symptoms, 4 Questions
Amobarbital sodium vs. placebo	$p=0.1$	$p=0.2$	$p=0.2$	...
Meprobamate vs. placebo	$p=0.1$	$p=0.01$†	$p=0.01$†	...
Prochlorperazine vs. placebo	$p=0.2$	$p=0.4$	$p=0.2$	$p=0.1$‡

* No significant differences in somatic side-reactions were observed.
†Significant at 1% level of confidence.
‡Significant at 10% level of confidence.

instrument for measuring change if the patients are (1) able to answer the questions and (2) sufficiently motivated to complete it properly.

Comment

Questionnaires, over-all ratings of clinical impressions, and the patient's own daily evaluation are some of the methods used in studies of outpatients, but rarely has an effort been made to compare different methods of evaluation with each other, or to break down questionnaires into various symptom clusters. Our study, however, is focused on cluster and item analysis, as well as on a comparison of results achieved with different methods of evaluation.

By means of a questionnaire, divided into subscales, we attempted to record and categorize the distress of individual patients along traditional lines of clinical symptomatology. We want to make it explicit, however, that our subscales do not by any means represent a selection of questions designed to test the effect of several drugs on such diagnostic groups as anxiety states and depression; rather, they represent symptom complexes which are most often found in anxious, neurotic patients.

When setting up this study we did not weed out placebo reactors, although we were aware that inclusion in a study of a great number of these may dilute drug effects and devaluate the study itself. We found, as mentioned under "results," that the placebo effect was most marked after the initial contact with the physician in the first two-week period. As the study continued, and as patients became aware of the efficacy of some of the more active drugs, the inert placebo became less effective. Other factors probably played a role, but one important factor stood out, namely, that the initial contact with the physician produced significant changes in the patient's feeling of well-being, no matter what kind of drug was given to him. Thus, our study confirmed that the placebo effect, which includes such variables as external environmental changes, the patient-doctor relationship, and others, and not the mere "giving of medicaments," is quite marked in neurotic patients. Often patients presented tainted reports during the first several weeks, overemphasizing improvement. As time went on, these effects wore off. Because of the particular design we used, we cannot omit the first two weeks from statistical evaluation, and therefore must bear in mind that all three active drugs were probably more effective than our data show.

Concerning some of the differential effects produced by therapy with meprobamate and prochlorperazine, we feel that the beneficial effect of meprobamate on insomnia cannot be attributed primarily to a sedative effect alone, since hardly any clinical sedation occurred. One might speculate that the muscle-relaxing property of meprobamate may be responsible for the favorable response. By relaxing tense muscles, meprobamate frees tied-up energy, diminishes proprioceptive stimuli, and allows natural sleep. This theory is supported not only by pharmacological studies and the statements of patients that they hardly ever experienced hangover after taking meprobamate but also by the fact that best results usually are achieved when patients take meprobamate regularly during the day, and not just at night. Relief of insomnia without heavy sedation has an important bearing on the outcome of drug treatment in many patients. Neurotic patients, particularly those with an obsessive-compulsive character make-up, are often frightened by the hypnotic effect of a drug and fear they might lose control over themselves. Apparently the alleviation of insomnia quite often breaks a vicious cycle and allows the patient to integrate his ego functions better. If this process is accompanied by further reduction of proprioceptive (muscle) stimuli, as well as by some direct effect on the diencephalon, efficacy of the drug increases.

Other interesting differential drug effects are that of meprobamate on irritability and that of prochlorperazine on gastrointestinal symptoms caused by anxiety. Inspection of the data "patient's first choice" shows that the 17 patients favoring meprobamate showed most improvement in the cluster scores for insomnia, depression, irritability, and anxiety, while the 7 patients favoring prochlorperazine showed most improvement in the gastrointestinal and anxiety scores. The differential effect of prochlorperazine on the gastrointestinal scores is quite obvious. While meprobamate influenced a patient's response on the gastrointestinal score randomly and only mildly, prochlorperazine improved the gastrointestinal scores of six out of seven patients. Amobarbital sodium was favored by only three patients, and no consistent pattern of relief of symptoms could be seen.

Our data further show that (1) a patient's own choice, (2) results of cluster and item analysis, (3) number of returned capsules, (4) pattern of "drop-outs," and (5) over-all analysis, as measured by the relative and absolute rating scale, correlate quite highly. They all point in the same direction, and all place the drugs in the same order of efficacy, that is, meprobamate, prochlorperazine, amobarbital sodium, and placebo.

The change in total scores of the clinical questionnaire did not necessarily correspond to the change in over-all rating. In fact, often a patient showed no change or only little change in the total questionnaire score but still felt, and often was judged so by the examiner, much improved. A few times it also happened that a patient, despite the improvement scored in the questionnaire, did not feel better. Possible explanations for this may be that patients having a number of neurotic signs and symptoms usually are concerned primarily with only one or a few symptoms, i. e., gastrointestinal symptoms, heart palpitations, insomnia, and others. If such a patient finds relief from his "chief complaints," he will feel much better and may function more effectively despite the fact that he still suffers from many other neurotic symptoms and signs. On the other hand, a patient who has lost most of his symptoms but whose chief complaint persists will report no change in status.

A study of the histories of the two groups of participants in the study who dropped out leads to the impression that those who drop out early in treatment are persons whose symptoms are ego-syntonic, with the result not only that their illness represents an established way of life but that their symptoms may provide a large measure of secondary gain. One might speculate that those subjects who drop out only after a prolonged period of treatment might profit from psychotherapy, because they do not have the same degree of pathological motivation by secondary gain.

Another point of interest was the investigator's reaction to the patient, particularly whether his feelings tended to influence results. Both physicians noticed that they had to restrain themselves from rating a patient as more anxious than he actually was during the first visit and less anxious than he actually was during later visits. Both physicians tried to grade objectively, but it is possible that, especially in subsequent visits during the course of the study, they might have tended to give a lower score if any doubt as to degree of severity of symptoms was present.

Transference feelings too must have played a role. Both physicians saw some patients whom they liked, some about whom they felt indifferent, and others who irritated them. Both physicians liked or felt irritated instantly by certain patients, while their liking or irritation for other patients developed gradually as an interplay between patient and doctor. However, none of these three feelings experienced by the physician greatly influenced the patient's improvement. Both physicians' feelings toward a given patient correlated quite highly. We could not confirm the findings of Uhlenhuth and associates [1c] that two physicians achieved quite different therapeutic results with the same drugs in the same experimental setting. In our study we found that the percentage of patients improving under a given drug condition was roughly the same for both physicians.

Summary

Fifty-one patients participated in a double-blind evaluation of the efficacy of amobarbital sodium, meprobamate (Miltown or Equanil), prochlorperazine (Compazine), and placebo in treatment of neurotic symptoms. They represented a heterogeneous group of medical outpatients suffering from a variety of neurotic signs and symptoms. Twenty-eight patients concluded the study by taking all four medicaments in random order. Each drug was given for two weeks four times per day, in the following doses: amobarbital sodium, 30 mg.; meprobamate, 400 mg.; prochlorperazine, 5 mg.; and placebo. All medicaments were administered in identical and coded capsules.

The following methods of evaluation were used: relative and absolute over-all improvement scales, filled out by both the patient and the physician separately; Duke check list, filled out by the patient; clinical questionnaire with 45 questions, each question graded on a four-point scale, filled out by the physician; and Taylor manifest anxiety scale and Saslow screening inventory administered twice, once at the beginning and once at the end of the study.

Our main findings were as follows: 1. Over-all analysis of variance, with use of total scores of the clinical questionnaire, indicates that all three active drugs and also the placebo influenced patients significantly, irrespective of order and sequence of drug administration. All other tests, however, when compared to the period prior to therapy, showed no significant change with use of placebo, while all of them showed significant change with use of meprobamate and prochlorperazine and most of them also with use of amobarbital sodium. 2. Therapy with meprobamate always produced the more marked change toward improvement and most often showed a significant difference between drug and placebo; prochlorperazine and amobarbital sodium produced less over-all change. 3. Analysis of several subcategories and items of the questionnaire showed that the effect of meprobamate was significantly better than that of placebo in the case of the irritability ($p=0.01$), depression ($p=0.01$), and insomnia ($p=0.005$) clusters. Statistically, the efficacy of prochlorperazine in the gastrointestinal score was barely significantly ($p=0.1$) better than that of placebo. However, more weight should be added to this finding, since only a small number of our patients had gastrointestinal symptoms. Amobarbital sodium showed no differential effect in any one of these clusters or items. 4. A patient's preferred choice of a drug, as well as his own evaluation of the degree of improvement he experienced, did not always correspond with total questionnaire scores. His judgment was influenced greatly by disappearance or recurrence of "main symptoms."

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3600 Spruce St. (4) (Dr. Rickels).

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GENERAL PRINCIPLES IN TREATMENT OF INJURIES TO ATHLETES

Don H. O'Donoghue, M.D., Oklahoma City

The joint session to consider the treatment of injuries to athletes is an indication of the tremendous interest in this subject which has mushroomed in the past few years among the physicians of the United States. A few years ago a discussion of injuries to athletes at a national meeting was a rarity. In the last few years there has burgeoned a wealth of sessions taking up various aspects of this subject. Our own American Medical Association had a special program on this subject at the San Francisco meeting a year ago. The American Academy of Orthopaedic Surgeons presented a panel on athletic injuries at their annual meeting this year and expect to continue this program in 1960. The number of meetings held on a local level is legion. State society meetings and postgraduate courses on this subject are available all over the country. (In Oklahoma there is a joint effort on the part of the state chapter of the American College of Surgeons and the Oklahoma State Medical Society designed to improve the treatment received by athletes at a high-school level.) This enthusiasm is shared by trainers, coaches, physicians, and specialists alike and is resulting in a vast improvement in the management of injuries to our youth.

Experience has led to the conviction that a physician called on to treat an injured athlete should respect the patient's desire for early return to a competitive status. The physician's examination should be thorough, and treatment from the beginning must aim at the complete rehabilitation of the athlete.

Value of an Athletic Program

Organized athletics has been gradually extended to involve a greater segment of the youth of our country. In many areas not only the junior high but the grade schools participate in competitive sports. Whether or not one agrees this is good, it must be recognized as a *fait accompli* which cannot be ignored. There is no present trend toward less athletics; rather, the trend is toward a more inclusive program. Since one of the major criticisms levied at athletic programs has been the limitation in the number of participants, many of the athletic programs are making deliberate efforts to include greater numbers, so that in many schools all of the students participate in one way or another. In the United States the various types of organized ath-

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Read in the Symposium on Athletic Injuries before the Joint Meeting of the Section on General Practice, the Section on Orthopedic Surgery, and the Section on Physical Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959.

letics, many of them competitive, must serve the whole function of physical education, whereas in other countries there are health clubs, hiking clubs, and ski societies. (This latter type of organization has not been accepted in the United States. Our citizens are a keenly competitive group, and exercise for exercise's sake, calisthenic drills, and regimentation into marching clubs have not been popular here—one reason being that in other countries these various groups have been used as springboards for political indoctrination, not always of a desirable type. Our young people have an almost paranoid distaste of anything that smacks of regimentation.) Our effort, therefore, must be not to decry athletics and demand less participation but, on the contrary, to demand greater participation and then see to it that the whole background of organized athletics is improved.

Competitive athletics has a great appeal to most Americans. However, the major interest has been directed away from those factors which make athletics most valuable. The public is more inclined to watch the score or cheer the outstanding player than to direct its attention toward those facets of the program which are calculated to return the most good to the greatest number. Comparatively little attention has been paid to either the conditioning of the athlete or the prevention of his injury. An outburst of righteous indignation may follow the untimely death of a budding prep-school player. The sports pages eagerly play up injury to the star. A personal experience by its author will often trigger a lay magazine article on the importance of proper equipment and on the value of physical conditioning as factors in the prevention of injury. In the final analysis, however, the public and, I fear, the majority of the medical profession, has little information on the actual processes of training and little knowledge of the actual mechanics of injury. One may presume that such a group as this audience has both a major interest in and information about these subjects. However, we have much to learn from our colleagues in the training room, with regard to conditioning and equipment.

Benefits of Athletics

Why is it important for young men to participate in athletics? There are many quaking parents who feel, at times, that the solution to the problem of athletic injury is to abolish competitive athletics, particularly contact sports. Therefore, it is up to us to demonstrate the true tangible values of athletic competition, in order to justify participation in an activity which does carry an element of risk. Are there true tangible benefits to be derived from athletics? Some of the benefits of athletics are obvious. No one seriously doubts that the athlete develops a stronger, healthier body. Most of the myths of catastrophic sequelae from strenuous athletic activity have been dispelled. I think most of us agree that participation in competitive athletics has a salutary effect on the character of the participant. This is particularly true if the programs are so managed that too much emphasis is not placed on winning and more emphasis is placed on the vital ability of the athlete to value his own and respect his opponent's capabilities. The player learns the value of team participation, that he must sacrifice immediate gain to the final end, and that desire is one of the most important factors in success. There are material benefits, also, in our present educational system. Many a young man goes to school on his athletic ability. Who is to say that the athletic scholarship is not as worthwhile as the scholarship for merit in other fields? In most of the better schools the scholarship athlete maintains a scholastic average higher than the average of his school.

So much for the benefit of athletics for the student in school. What about after graduation? There is an increasing tendency for the athlete to stay in a related field after graduation. Conditioning of our youth depends on the organized type of athletic training which they get in the elementary and secondary schools and through such organizations as the YMCA and the Boy Scouts. Without the trained athlete these programs would be hard put to provide capable leaders. We need these people. Indeed, we will find that much of the education of our youth is in the hands of the former college athlete.

Why, then, is there such bitter opposition to organized competitive athletics as such? Because of one principal thing, namely, physical injuries. This is almost the only real objection to the athletic program. Our youngsters do on occasion get seriously and even fatally injured. It must then be the duty of the medical profession to do everything in its power to minimize the things which interfere with the goals of the athletic program.

Role of the Physician

What can we do to prevent injury, to minimize temporary disability, and to prevent permanent disability? Much has been accomplished toward these ends. A few years ago the trainer in the average scholastic institution was a fugitive from the supply room, having promoted himself into the "wrapping and taping club" largely by osmosis. He had no real knowledge of injuries. Too often immediate playing was the major consideration rather than the final goal of complete recovery of the patient. During this era the doctor was a necessary evil. The player felt that once he reached the doctor his days as an athlete were over. In too many instances this feeling was justified, for two reasons. First, since the doctor was the last resort, he did not see the player at the time he could do the most good. Second, to the doctor the fact that the player was an athlete or should be able to remain one was not of immediate concern. Many times the first recommendation the doctor made was, "Give up football." This tended to confirm the conviction of the player, the coach, and the public that the objectives of the athlete and the physician were incompatible.

In our major institutions this is no longer true. In the well-run athletic program of today, the coach, trainer, team physician, and specialist all combine in one effective unit, designed to bring the player to top condition and to keep him there. In fact, more emphasis is placed and actually more time is spent on preparing a player to participate and on preventing his injury than is spent on treatment. The time when the player, coach, trainer, and physician are all working at cross purposes is rapidly becoming a thing of the past in our better institutions. Athletic injuries are much less frequent than in the past. Injuries are less severe. The period of disability is shorter. The degree of recovery is more complete. Many factors have combined to cause this vast improvement in the one area where it must be conceded that athletics may have a bad effect.

So, once again, the physician must become not only the doer but also the teacher. The orthopedist must prepare himself to handle injuries and he must pass this information on to the team physician, who is in the final analysis the major component in the management of the athlete. There is one overriding difference in the management of injuries to athletes from that of any others; that is, that the patient must completely recover from his injury or he is no longer an athlete. True, this should apply to any injury the doctor sees; but nowhere is it dramatized so constantly as in the care of the athlete. While prevention of injury is important, the major emphasis must be placed on treatment.

The most important consideration in the treatment of athletic injury is early detection, not only of the nature of the injury but of its degree. The optimum time to examine an athlete for injury is as soon as possible after he is hurt. It may be impossible to examine the patient or to make a complete diagnosis at this time, but if it is possible precious time has been saved. Frequently the initial examination is by the coach, trainer, or physician on the field. Whoever this is, he must make as careful an evaluation of this player's condition as he is capable of doing and must pass this information on to each succeeding link in the chain of therapy. The doctor must conscientiously and objectively examine the player. This is no place for wishful thinking. The player is eager to continue and should not be deprived unnecessarily of this privilege. However, if continued competition will add to the hazard of his injury, he should not be permitted to compete. It is always better to err on the side of conservatism.

After the injury forces the player to the sidelines, what then? The prevalent habit of packing the injured part in ice and delaying examination until a convenient time the next day or so is to be deplored. Your examination as a physician should be done at the earliest possible moment, even at inconvenience to yourself, the coach, or the player. The part should be undressed, all taping or strapping removed, and a real examination done. Frequently, the diagnosis, which will be easy if done early, becomes exceedingly difficult later, since pain increases apprehension and swelling, edema, and hemorrhage interfere with an accurate evaluation of the injury.

Once treatment is decided on, the physician should proceed to carry it out with confidence. If it is something the team physician should treat, he should be encouraged to do so. If the specialist's attention is required, the specialist himself should not hesitate to say so. The physician should be encouraged to seek the specialist's advice early, and this can be done only if rapport with the orthopedist is such that there is fullest cooperation between player, referring physician, and specialist. I have found the following concepts of treatment to be of great value.

Concepts of Treatment

1. Recognize the value of competitive athletics. The physician must believe that to this particular patient it is vital that he be restored to competitive athletics. If he fails in this, the patient-doctor confidence becomes lost. The doctor who deprecates the player's ambition should not be treating him.

2. Avoid expediency. Outside influence must not be permitted to outweigh sound medical judgment. Many factors will tend to influence the doctor's decision. All concerned are extremely unwilling to believe that the player is really hurt. The boy's desire to compete, his fear of failing his teammates, the parents' desire to see their son excel, the coach's hope that the player is not really hurt, all must be ignored if the proper conclusion is to be reached. Procrastination, vacillation, or so-called conservative attitudes must not prevail. Temporary convenience must be abandoned for the ultimate goal.

3. Adopt the best method of treatment. Medical evaluation of the nature and extent of injury must be the controlling factor in deciding what treatment to employ. A temporizing attitude will not accomplish the best results. If you really believe that one method is distinctly better than another you should carry it out. This must be an entirely objective decision. How often do we hear, "Well, perhaps this knee would be better operated on, but I put it in a cast"; or "We really should have put the boy on crutches but. . . ."

4. The treatment must be prompt. A definitive decision about the proper method of treatment must be made at the earliest possible moment and then carried out.

5. Recovery must be complete. While this may not always be possible in any given case, 100% rehabilitation must be the goal. The athlete is

basically in good condition and can well tolerate any reasonable measure if it serves to increase his chances for a complete recovery.

Will such a program be accepted? Yes, but not without some time and effort on the part of the doctor. He must be able to show conclusively that the program is better, not for himself, but better for the school, the coach, and especially the player. This may require some educational effort. It will require time. The doctor himself must be prepared to cooperate fully, with interest and ability. As the doctor's program is improved, those most concerned will note the results. They will observe that the sprained ankle responds to treatment and that a short complete lay-off is followed by normal ability, as opposed to an ineffectual season. The coach will observe that prompt treatment restores the player more rapidly, permits more actual playing in the long run, and so is better for all. The player will not fear the doctor who has a sympathetic and understanding attitude. He notes that his buddy gets well. He also expects to get well and will accept the physician's recommendation for treatment. He may fear some specific part of the treatment, such as the insertion of a needle into a joint, but not to the extent of failing to return or refusing the treatment, provided he believes that you believe in restoring him to his normal ability.

1111 N. Lee St.

BASEBALL SHOULDER

Rex L. Diveley, M.D.
and
Paul W. Meyer, M.D., Kansas City, Mo.

Systematic observations, including routine roentgenograms of the shoulders and elbows, have been made on a number of pitchers through two seasons of baseball. Comparison of the right arm with the left was found essential. The characteristic roentgenographic features in cases of baseball shoulder were calcific deposits about the origin of the m. triceps brachii on the margin of the glenoid fossa of the scapula and osteophytes or loose bodies or other signs of irritation about the lateral epicondyle of the humerus and the olecranon process of the ulna. Other possibilities suggested by physical examination are fraying of the supraspinatus tendon and partial rupture of the origin of the m. triceps brachii. Accumulating experience correlated with systematic studies should help to determine the prognosis when baseball shoulder develops in a player and should enhance the value of preemployment examinations in recognizing the arm that is likely to be disabled by the extreme stress of pitching.

Bennett[1] in 1947 called attention to the fact that extreme overexertion of throwing a baseball could and often did cause certain pathological changes in the shoulder or elbow, or both, in professional baseball players. This condition is most often noted in the throwing arm of the pitcher, since he makes a continual super-effort with the arm and shoulder in a forward extended position, and the forearm is twisted or rotated to produce a curve to the flight of the ball.

Bennett noted the following common pathological lesions in pitchers and other baseball players: (1) a deposit on the posterior and inferior margin of the glenoid fossa of the scapula, on or about the origin of the triceps brachii muscle; (2) irritations about the external condyle of the humerus and osteophytes or loose bodies about the tip of the olecranon or external condyle of the humerus, or both; and (3) fraying of the supraspinatus tendon. The author noted that the second and third findings are not distinctive to baseball players but may be found in any patient with an ailing shoulder or elbow.

The art of pitching brings into play an extreme extension action of the triceps brachii at the elbow, with a rotary action of the forearm and a flexion of the wrist. This continued super-effort causes an irritation or partial rupture, or both, of the origin of the triceps muscle on the infraglenoid tuberosity of the scapula. Again, this continued extension action

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From the Dickson-Diveley Clinic.

Read in the Symposium on Athletic Injuries before the Joint Meeting of the Section on General Practice, the Section on Orthopedic Surgery, and the Section on Physical Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959.

of the triceps at its insertion on the olecranon of the ulna may cause an irritation of the periosteum at this point, or even a calcific deposit. In older patients, with chronic cases, there may be evidence of bone spurring or osteophyte formation on the olecranon. Also, the extreme and forced action of forearm rotation, in either pronation or supination, and forced flexion and extension of the wrist—the motion involved in throwing a curve ball—may and generally does cause an irritation of the internal or external condyle of the humerus, with a subsequent bursitis, later osteophyte formation, and even fragmentation at the origin of the forearm muscles on these prominences.

In the case of the sore shoulder, the player complains of a general soreness in the shoulder joint which is aggravated by throwing and is relatively painless when the shoulder is immobilized or rested at the side in a sling. When the shoulder is examined, a point of tenderness can be ascertained on deep palpation in the posterior aspect of the axilla. If the arm is forcibly extended at the elbow by active motion, the pain is reproduced in the shoulder and is noted deep in the region of the axilla.

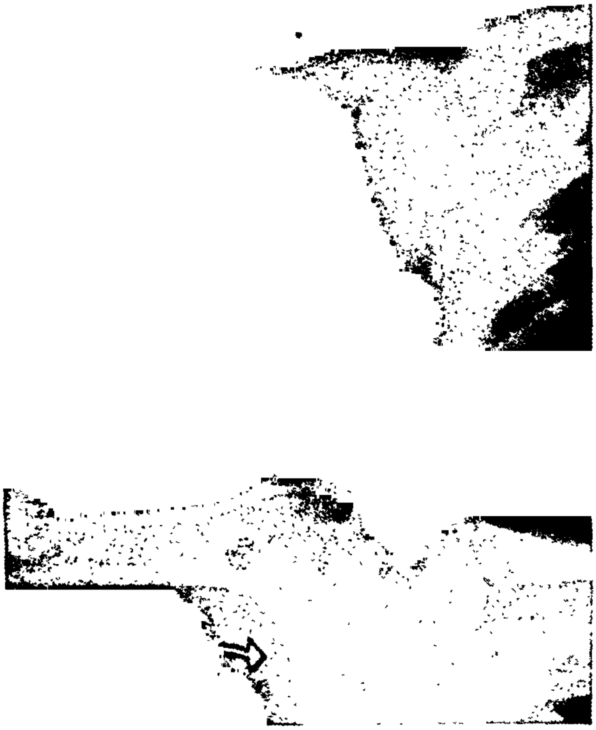

Fig. 1.—Roentgenograms of *top*, normal shoulder, and *bottom*, shoulder with shadow of calcific deposit on inferior rim of scapular glenoid from same patient.

An anterior-posterior roentgenogram taken with the arm in a midabducted position will bring into clear view the inferior margin of the glenoid of the scapula. The opposite shoulder should be observed in the same position for comparison (fig. 1). The pathological changes found may vary from a slight periosteal irritation on the inferior margin of the scapular glenoid to a large calcific deposit, and in older patients, with more chronic cases, definite spur formation or other osteophytic changes.

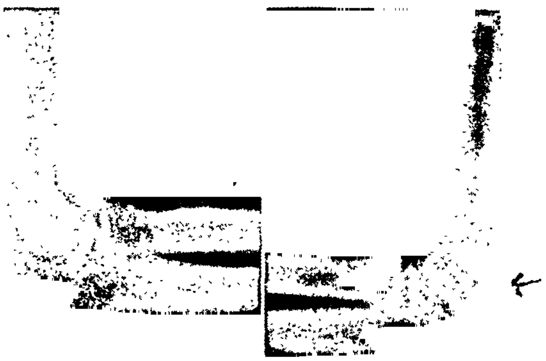

Fig. 2.—Roentgenograms of *left*, normal elbow, and *right*, elbow with calcific deposit on tip of olecranon from same patient.

If the point of tenderness is localized over the outer tip of the shoulder and along the course of the supraspinatus tendon, one should suspect a tear of this muscle, with a resulting calcific change in the muscle or tendon, or both; or one may suspect a subdeltoid bursitis in this region with or without calcific deposit in the bursal sac. Roentgenograms of the shoulder often reveal a calcific deposit over the outer tip of the joint. If the point of tenderness is noted on the anterior tip of the shoulder, roentgenograms of the shoulder, with the arm in external and internal rotation, should be taken. In external rotation the anterior bursal sac will be thrown into relief.

In the patient with the sore or painful elbow the point of tenderness will be localized over the tip of the olecranon or over the internal or external condyle of the humerus. Roentgenograms should be made of the ailing joint in the anterior-posterior and lateral planes and of the opposite or normal elbow for comparison (fig. 2). One may find a periosteal irritation, osteophytic changes, or even fragmentation at the insertion of the triceps into the olecranon or on the internal or external condyle of the humerus, the latter being the points of origin of the forearm muscles which rotate the forearm and hand and flex the wrist, all of which actions are used in the throwing of a curve ball. Not all cases can be confirmed by roentgenography, but most will elicit a definite point of tenderness which should differentiate the diagnosis.

In the player with a definite tender area in the posterior deep axilla, with or without a calcific shadow, a diagnosis of a partial rupture of the origin of the triceps brachii can be made. These patients will generally respond to treatment, but in chronic cases this response may be greatly prolonged. After the tender area has been well localized 2 cc. of hydrocortisone (Hydrocortone) is injected in the area from behind the axilla. One should be careful to introduce the needle along the rim of the scapular glenoid and avoid the area below the axilla where the great vessels and nerves are found. The arm is placed at complete rest in a sling and the injection repeated in five days. After two weeks, if the pain has subsided, motion in the shoulder may be started and increased in proportion to the lack of symptoms.

In the case of localized tenderness on the outer or anterior tip of the shoulder, the area of point tenderness should be injected as described above and rest and motion carried out in a like manner. We have found that, when the tenderness has been localized with the needle point, a small amount of the solution should be injected into the area, then the needle point should be withdrawn slightly and the adjoining areas injected in turn; in other words, it is difficult to inject the exact point of tenderness, and the surrounding areas should be infiltrated. In most patients, even those with a calcific deposit, the pain and discomfort can be relieved and, in many cases, a large part of the calcium deposit may be dissolved or absorbed (fig. 3).

In patients with lesions about the elbow, the areas of point tenderness should be injected with 1 to 1.5 cc. of hydrocortisone over a period of two to three weeks, with partial rest to the joint. In the case of a ball player, the elbow should be completely rested for two weeks. One-half to one cubic centimeter of procaine (Novocain) may be added to the hydrocortisone; this will, in a large measure, allay immediate reaction to the injection. It has been our experience that only in extreme cases should excision of the calcific sac, bony spurs, or fragments be advised.

During the past two baseball seasons, we have taken routine roentgenograms of the shoulders and elbows of all pitchers on the Kansas City Athletics and, in several cases, have noted an irritation over the infraglenoid tuberosity, even before the onset of symptoms, which we feel is the forerunner of a definite pathological change. If careful treatment and observation are practiced in these early cases, we have found, many patients can be salvaged before their shoulder injuries become chronic. It must be stated, however, that the conditions of two patients with a definite deposit in the infraglenoid rim, whose progress we have been following for two seasons, have gradually grown worse, and the pitchers have been sent to the minor leagues.

The preemployment examination is most important. If, by roentgenologic and physical examination, a deposit, fragmentation, or joint tenderness is noted, our club is not encouraged to invest a great amount of money in the player's training, and the condition is at least carefully observed, protected, and treated or the player's position changed. It is hoped that, with more experience in these routine examinations, we can establish criteria for the arm which is liable to break down under pitching stress and strain.

These views and observations are given not only to confirm Bennett's original thesis but also to call attention to this condition again so that we may all make a more thorough study of these pathological changes. We believe that with the advent of hydrocortisone and its derivatives, a treatment has been found for these pathological conditions of painful shoulders and elbows, with which we may be able to salvage a great number of these athletes for further profitable service.

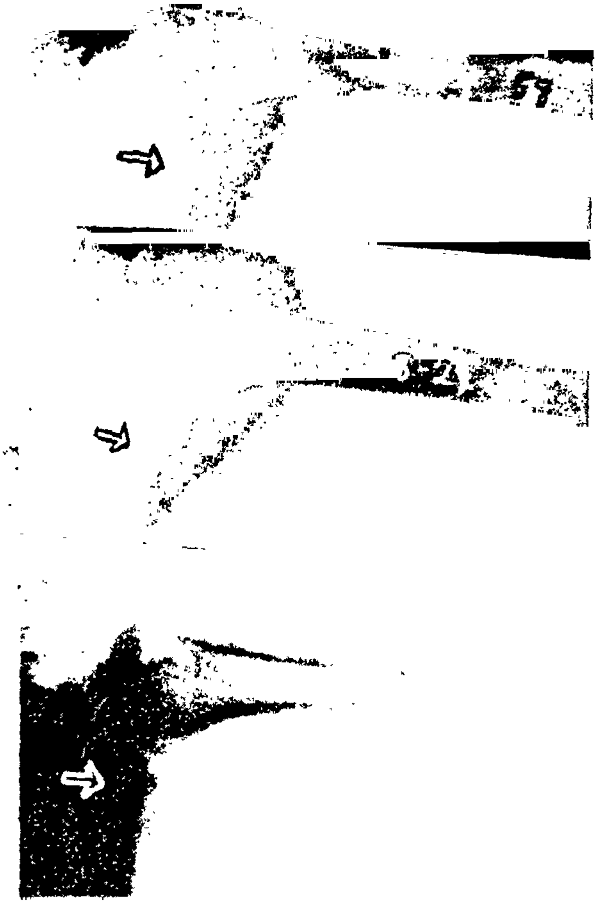

Fig. 3.—Roentgenograms of shoulder with calcific deposit of patient under treatment. *Top*, deposit was large, with round edges. *Middle*, four months later deposit had become smaller, spur-like shadow. *Bottom*, nine months later patient was asymptomatic.

4312 J. C. Nichols Pkwy. (11) (Dr. Diveley).

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REHABILITATION OF KNEE MENISCUS INJURY WITH ASSOCIATED MALACIA OF THE PATELLA

Donald R. Lannin, M.D., St. Paul

Degenerative changes in the articular cartilage of the patella probably occur earlier and more constantly than in almost any other joint surface. The incidence of the degenerative change and the time of its onset may vary a great deal. However, probably by the age of 30 years everyone is affected to some degree. Bennett and co-workers[1] have demonstrated that after 15 years of age every person may show some evidence of degeneration in the knee joint and that the superficial articular cartilage layer of the patella is the area of earliest change. In addition to the normal degenerative changes injury, particularly through athletics, is a major factor in the incidence of malacia of the patella.

I have reviewed 294 arthrotomies performed on athletes and have attempted to evaluate the effect of associated chondromalacia of the patella. All of these operative procedures were performed by me and the conclusions represent purely personal impressions. These were all performed on male athletes between the ages of 16 and 26 years. In every case the preoperative diagnosis was a tear of either the medial or the lateral meniscus. All cases involving a preoperative diagnosis of fracture, osteochondritis dissecans, ligamentous injury, or actual grade 3 chondromalacia of the patella have been excluded. The degree of posterior patellar crepitation, representing chondromalacia of the patella, has always been included as a preoperative physical finding, and the incidence and degree of actual patellar changes found at surgery have been recorded later.

Several similar systems of evaluation of patellar changes have been given by Cave and Rowe,[2] Wiles and co-workers,[3] and later by O'Donoghue.[4] Because of the size of the incision used at the time of arthrotomy, little actual visualization of the posterior surface of the patella is possible. Most impressions have been gained by palpation.

In only seven of the cases has a patella been felt which showed no evidence of any degree of softening. In 76 cases softening of some area but no fissure formation or fragmentation was demonstrated. Of the more severely involved cases an attempt has been made to separate the patellar changes into two groups. Grade 1 represents those patellas with softening, minimal to moderate fissure formation, and a definite localized area of irregularity of the surface. Grade 2 represents those patellas with extensive areas of multiple fissure formation and stellate fissuring and those having areas of completely separated cartilage. On the basis of this method of classification 103 cases, or approximately 35%, have been allocated to grade 1 and 108 cases, or 37%, have been classified as grade 2.

Thus, in a total of 211, or 72%, of the 294 cases there were degenerative changes in the articular surface which I believed were severe enough to affect the after-treatment and the prognosis for recovery. This represents a considerably higher percentage than the 48 of 166 cases reported by Wiles and co-workers.[3] It is also interesting that 21, or slightly over 20%, of the patients with grade 2 cases also showed some pitting of the intercondylar groove of the femur, usually in a point roughly corresponding to the irregularity of the posterior aspect of the patella. At the time of meniscectomy it has been my practice to remove portions of the articular surface of the patella which are actually loose but to leave undisturbed any areas of softening or ordinary fissure formation.

The main objective in rehabilitation of the patient with knee injury is either the maintenance or the restoration of quadriceps strength. Other muscle groups such as the hamstrings improve easily and spontaneously. Quadriceps exercises allowing a full range of motion of the muscle group are preferable for quick rehabilitation; however, it is possible to develop excellent quadriceps strength and at the same time keep the irritation from malacia of the patella to a minimum. This malacia is a major factor in irritation of the knee and in production of effusion of the joint. Quadriceps exercises in which the knee is extended from a flexed position tend to increase this irritation and increase postoperative effusion (fig. 1). Probably in the cases of grade 1 malacia, and certainly in the cases of grade 2 malacia, a special effort should be made to carry out the quadriceps exercises with a minimum of flexion of the knee and with a minimum excursion of knee motion.

The program for maintenance or restoration of quadriceps strength in these operative cases is actually started preoperatively. The day before the surgical procedure each patient is instructed in quadriceps setting and in straight leg-raising exercises, with the knee kept in full extension. The afternoon after surgery, or at the latest the next morning, the patient is started on a program of raising the leg with the knee completely straight for periods of five minutes out of each hour. As soon as the pa-

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tient can carry out this exercise well (which usually takes only 24 hours) he is allowed to be up bearing *full weight but always keeping the knee in a fully* extended position. At the end of 10 days ordinary flexion is started and encouraged, but even at this point all quadriceps exercises continue to be performed with the knee in full extension. Weight-resistance exercises are started at the end of about two weeks and are carried out with the patient lying on his back and raising the leg with the weights attached to his foot for progressively longer periods (fig. 2). By the use of this postoperative program the excursion of the roughened patella through the groove of the femur is kept to a minimum, and the irritation and postoperative effusion are also kept to a minimum.

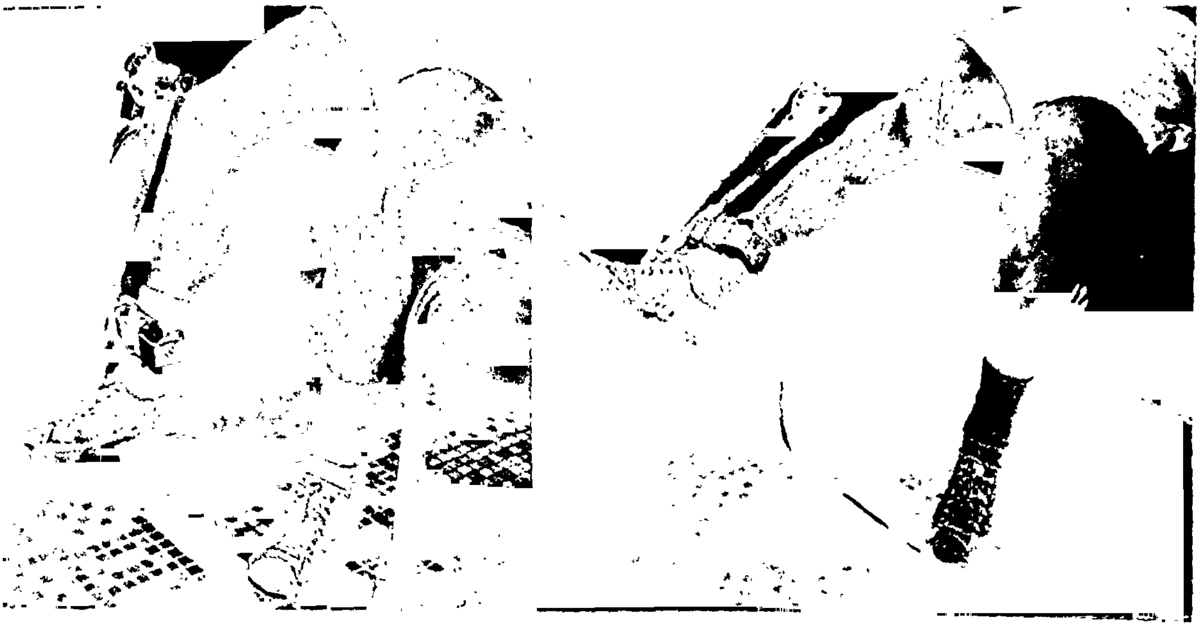

Fig. 1.—Example of incorrect type of rehabilitative exercise in patient with knee injury and associated malacia.

The choice of postoperative dressing is also influenced by the degree of malacia of the patella. Any type of circular dressing, even including an Ace bandage, which is worn during periods when the knee is being flexed, tends to increase difficulty. If the dressing is tight enough to force the patella into the irregular groove, not only will the patient have increased pain but the entire program of rehabilitation will be retarded. The use of an Ace bandage in any knee injury with an associated crepitation of the patella is probably contraindicated.

The catching sensation still produced by the malacia of the patella is one of the most common complaints present after arthrotomy. Many patients believe that removal of a meniscus will entirely do away with any feeling of catching or clicking, and the persistence of the malacia difficulty is a source of annoyance to them.

The progress of enough patients with grade 2 malacia has been followed to give the impression that, if there is no reinjury, there is some tendency toward spontaneous improvement. There is, of course, no real regeneration of superficial cartilage, and improvement is probably associated with me-

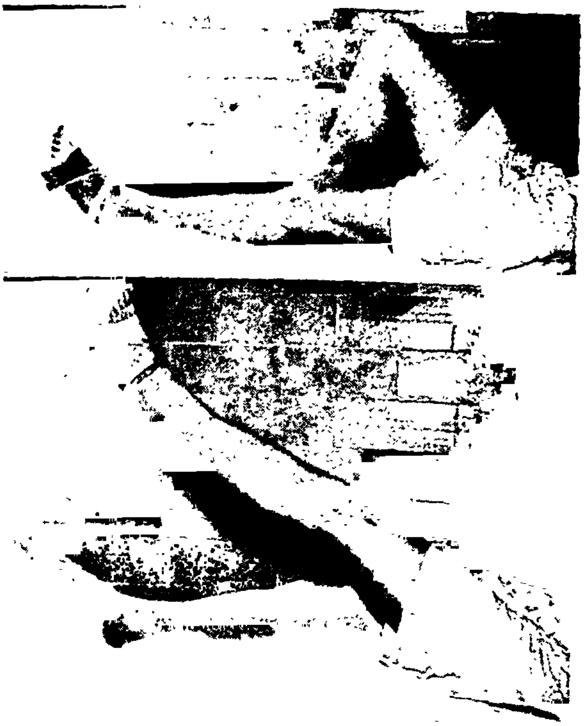

Fig. 2.—Example of correct rehabilitative exercise for patient with knee injury and associated malacia.

chanical smoothing-off of irregular areas. Not only do patients report that they have less of a catching sensation over a period of years but many times it has been possible to demonstrate on physical examination that posterior patellar crepitation which was present at the time of surgery is not present two years later.

Summary

The incidence of malacia of the patella associated with meniscus injuries of the knee is much higher than previously reported. This malacia is a factor in the postoperative management and requires special consideration in planning exercises for the restoration of quadriceps strength. In weight-resistance exercises the knee should be kept constantly straight and should not be brought from the flexed to the extended position.

942 Medical Arts Bldg. (2).

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BASIC AREAS OF PREVENTION OF ATHLETIC INJURIES

Robert G. Brashear, M.D., Knoxville, Tenn.

In recent years much has been said in the medical literature both for and against athletics in general and football in particular. Some authors extol football as a great builder of men, mentally, morally, and physically, while others condemn football, particularly because many of the injuries sustained playing football are carried over into later life. Football, however, must be accepted as an integral part of the American way of life, just as much as the automobile. Since we must accept athletics, it behooves us to find ways and means of preventing the most serious sports injuries.

There are three basic areas of prevention that the medical profession should be aware of, as both parents and physicians of the youth of America. The first, and probably the most important, is the selection of the coach. The head coach is the number-one preventer of serious injuries in athletics. He must be a morally sound teacher and leader. He must select the athlete, put him in his proper place, and teach him the various techniques of individual and team play, pitting boys of equal athletic ability against each other. By "drive, drive, drive and drill, drill, drill" he develops the strength and stamina to outlast the opponent and the skill to outmaneuver him. He prepares facilities. He buys protective equipment. He fits the equipment to the player and teaches him how to wear it properly. In all these ways, and in many others, he is actually preventing injury.

When films showing serious athletic injuries are studied, it becomes obvious that most serious injuries happen in a moment of poor coordination. Many coaches, realizing this, spend endless hours in trying to develop coordination in their players. With junior-high-school football developing more generally under improving supervision and coaching, the high-school and college athletes today are much better coordinated than in former years; at least, they can use their left hands. It is my firm belief that, unless a high school has sufficient funds to employ a first-class coach and to buy the best protective equipment, it should not be permitted to have football in its athletic program.

The second area to be considered is that of the team physician. In my state official regulations will not permit a football game to start until there is at least one doctor available on the field, not in the stands, and an ambulance is parked just off the field. This is considered a minimum basic requirement. When play begins, it is understood that all injuries necessitating "time-out" require removal of the injured player from the game. An immediate and complete examination of the injured athlete is made, with emphasis on the exact mechanism of injury. The attending physician makes the decision about the fitness of the player to return later in the contest.

The team doctor, the trainer, and the coaching staff form a well-coordinated team which can prevent many major injuries, particularly reinjuries. Having a physician present on the football field during a game is not sufficient. The modern concept

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of an athletic team doctor is that of a consulting physician who shares appropriately in organizing the athletic program. He is available not only for football games but also for consultation with the coach and trainer throughout the year. This is the ideal toward which we should work.

Making such arrangements is a real problem—a problem for organized medicine as well as for school officials. We physicians deliver all of these athletes. We treat them through infancy and childhood, seeing that they have the benefit of all the immunizing and other preventive modalities known to science. In my opinion, at this period of dangerous athletic participation we have a continuing obligation to serve and help.

The American Medical Association recognizes this problem and, through its Committee on the Medical Aspects of Sports, is actively promoting programs for safety in sports. Yet in many places coaches still find it difficult to work out arrangements for a team physician of the kind I have described. Young Americans can and do get good medical care when they are injured or ill, but medical controls are essential as an integral part of the high-school athletic program.

Let me put the matter on a personal basis. I urge each of you who is interested in athletics to take a high school under your wing by acting as athletic team physician. While this does require time, with little or no financial reward, remuneration comes in many other ways. Whether you know much about athletics is a minor point. As soon as you start working with boys and with coaches you will find you are well informed about most points on which the coaches need help.

The full-time athletic trainer, it seems to me, will become indispensable to the high school. Every college athletic program of any consequence now has a full-time trainer, and this has paid dividends. The day is rapidly approaching when high schools will recognize the value of having a trainer available. The reason high schools do not have them now is that there are no funds available for a trainer's salary. While many compromises have been devised, none of them is completely satisfactory. I would like to report briefly on the National Athletic Trainers' Association, of which I am an honorary member.

The N. A. T. A., formed in 1950, is a highly ethical group which now has over 500 members, all well educated and all intensely interested in prevention of athletic injuries. They meet annually and the theme of their meeting is the free interchange of information for the prevention of athletic injuries and diseases. They are aware of the fact that they need medical help and medical supervision. They have set up a committee for professional advancement made up of 13 well-known athletic trainers and 5 physicians who are deeply concerned with athletics. They have drawn up a college curriculum, which has been accepted by their membership and has been passed on by several well-known educators. This curriculum calls for a major in physical education and a minor in another teaching area, preferably one of the basic sciences. Obviously, to a person armed with a degree of this type, a teaching assignment and accompanying salary would be available almost anywhere. Thus, high schools could obtain the services of the teacher-trainers. In addition to this degree, the N. A. T. A. plans to have each member take an additional year of study in physical therapy, and their curriculum set up on this basis is acceptable to every physical therapy school in the United States.

A board of certification of trainers is now under advisement and will undoubtedly be developed in the near future. The National Athletic Trainers' Association today is made up almost entirely of college trainers and the trainers of professional athletic teams, who are participating in the practice of medicine just as surely as are x-ray and laboratory technicians. The main difference, as I see it, is that the trainers are not under appropriate medical jurisdiction. They need medical help and supervision; they have sought it and asked for it, and yet medical recognition, it seems to me, has been slow in coming to them. I believe the development of the professional athletic trainer and this National Athletic Trainers' Association is the greatest single advance in college athletics in the past 25 years. Its benefits should be extended to high schools at the earliest possible time.

603 W. Main Ave. (2).

CIRRHOSIS OF THE LIVER IN MEN AND IN WOMEN.—A review of 100 consecutive cases of cirrhosis of the liver in each sex showed that cirrhosis is largely postnecrotic in women and of the Laennec or so-called alcoholic type in men. The high incidence of postnecrotic cirrhosis in women is probably due to the fact that women are more susceptible to severe damage from viral hepatitis than are men. The greater frequency of Laennec's cirrhosis in men undoubtedly is due to the higher incidence of alcoholism among men than among women. Carcinoma of the liver is found more frequently in men who have cirrhosis than in women.— A. H. Baggenstoss, The Influence of Sex on the Pathologic Aspects of Cirrhosis of the Liver, *Postgraduate Medicine,* September, 1959.

KNEE INJURIES INCURRED IN SPORT

Thomas B. Quigley, M.D., Boston

Prompt, accurate diagnosis and treatment of knee injuries will prevent most of the "trick knees" of middle age. Examination must be thorough, orderly, and complete. Rupture of a ligament should be differentiated from sprain within a few minutes of injury, when diagnostic manipulation can be carried out without pain. Roentgenography is essential, not only to determine fracture or epiphysial injury but also to rule out unsuspected preexisting abnormality of bone. The most frequent injuries encountered are, in descending order of incidence, contusion, ligament sprain, meniscus injury, ligament rupture, and fracture or epiphysial displacement. Most meniscus injuries are accompanied by sprain, which should be allowed to heal before meniscectomy is advised. Immobilization produces muscle atrophy and should be kept to a minimum. Ligament rupture should be repaired promptly. Progressive resistance exercise is essential in convalescence. Protective taping to support the collateral and cruciate ligaments should be worn at each practice session and game for at least a year after any sprain.

There is probably a higher incidence of residual malfunction from knee injuries than from any other trauma sustained in sport. The middle-aged man with a "trick" knee dating from high-school or college days is commonplace. Most of these souvenirs can be avoided by common sense preventive measures, prompt diagnosis, and appropriate treatment.

Prevention

The best way to avoid injury in any sport is to become as skillful as possible in its performance. The gifted athlete or "neuromusculoskeletal genius" is rarely injured, and then only under freak circumstances. However, even ordinary persons can reduce their chances of injury to a negligible figure if they are well coached and do as their instructors tell them. This has been abundantly demonstrated on the ski slopes of the United States and Canada. Good execution of well-taught techniques requires a well-conditioned musculoskeletal system. No college student should indulge in a contact sport such as football, hockey, soccer, or lacrosse until he can sit on a table and extend his knee from 90 to 180 degrees, with a 50-lb. (22.7-kg.) weight fastened to the foot, 10 times within 40 seconds. The knee is no better than the muscles which cross it, and the player who cannot perform this test is inviting injury. No one should ski whose quadriceps muscles are too weak to support him for 60 seconds with his vertebral column against a wall, his hips flexed at 90 degrees, and his lower legs perpendicular to the floor.

The most important single factor in the prevention of knee or any other injury, for that matter, in sports is a careful physical examination.[1] Gross deformity, such as genu valgum (knock knee), genu varum (bow leg), genu recurvatum, inequality of leg lengths, limitation of joint motion, and muscular weakness from any cause, should preclude strenuous sport involving the lower extremities. Many abnormalities, however, can be corrected to the point of allowing safe participation. Most of these involve muscular weakness from previous injury and can be corrected effectively by a program of progressive resistance exercise.[2] Minor degrees of ligament instability can be protected by appropriate adhesive taping worn during the period of participation.

Diagnosis

Much can be learned from the history of the injury, particularly if the doctor knowns something of the sport. Even more valuable is direct observation, which should be the rule in all organized contests. The doctor himself should go on the playing field when he has seen an injury of potentially serious consequences occur. To leave to nonmedical persons such decisions as whether the injured player should continue to play or should walk from the field or be carried off is to gamble with permanent disability, with the cards stacked against the player. As a general rule, no one with a knee injury of sufficient severity to prevent further immediate participation in any sport should subject the joint to the added possible trauma of weight-bearing until the severity of the injury has been determined.

Examination must be thorough and orderly, with the patient in the supine position and his legs freed of clothing and equipment (fig. 1). Careful survey of the hips in adolescents is of great importance, since symptoms produced by displacement of the upper femoral epiphysis can be referred to the knee.

Assistant Clinical Professor of Surgery, Harvard Medical School; Surgeon, Peter Bent Brigham Hospital; and Surgeon, Harvard University Health Services.

· Read in the Symposium on Athletic Injuries before the Joint Meeting of the Section on General Practice, the Section on Orthopedic Surgery, and the Section on Physical Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959.

Roentgenography must be done, not only to reveal fracture or epiphysial injury but to determine the presence or absence of previously unsuspected abnormality, including osteochondritis dissecans, chondromalacia patellae, osteochondromatosis and other loose bodies within the joint, and even bone tumors and cysts.

Assuming that the knee and extremity generally was normal prior to the injury, the majority of sports injuries fall into five categories, either singly or in combination. These are, in order of incidence: contusion, ligament sprain, meniscus injury, ligament rupture, and fracture or epiphysial displacement.

Contusion.—Contusions of the soft tissues about the knee, while painful and disabling, are often minor. If full function returns within a few moments the player can safely resume his play or sport with a pad of foam rubber, covered with a stiff plastic, over the site of injury for protection from another possible injury at the same spot. Further treatment, if necessary, can await the end of the contest. However, if full function is not present and the player limps and is unable to perform well, to return to the game or sport is to court further and possibly more serious injury. In adolescents contusions often occur at the attachment of the infrapatellar tendon to the tibial tubercle. Discomfort is persistent, the tubercle is prominent and tender, and roentgenograms showing irregularity of the epiphysis are reported as indicative of "Osgood-Schlatter's disease."[3] This is now known to be not a disease but a minor abnormality of growth. Symptoms almost invariably disappear when activity is limited for a few weeks.

Ligament Sprain.—Sprained ligaments usually preclude further participation, at least on the day of injury. They are difficult to assay, from the point of view of severity, at the initial examination. The next day an accurate appraisal of the degree of sprain and a reliable prognosis can be made. However, the presence or absence of ligament rupture can and should be determined accurately during the 15 or 20 minutes after injury, when analgesia is still present and before muscle spasm has occurred. Manipulation of the tibia on the femur (fig. 1*E* and *F*) is diagnostic, and this short period may be the only time that such manipulation can be carried out, in a well-muscled young man, without anesthesia. If the tibia tilts 15 degrees or more when abducted or adducted on the femur in full extension, in comparison with the opposite uninjured knee, complete rupture of a collateral ligament is present.[4] If possible, a roentgenographic record of this abnormal mobility should be made by means of an anteroposterior film taken at the maximum of imposed valgus or varus.

Meniscus Injury.—Meniscus injuries result from a combination of torsion and abduction or adduction stress. Medial meniscus injuries occur 6 to 10 times as often as lateral ones. Injury to the meniscus is almost always accompanied by some degree of sprain. As a general rule it is well to allow the ligament injury to heal before making a definite diagnosis and condemning the meniscus to removal. On the other hand, there are cases in which the mechanism of injury is characteristic, roentgenograms show no bone abnormality, the last 15 to 20 degrees of extension are lost, there is no hamstring spasm, and tenderness is localized almost entirely to the joint line. In these cases the accompanying sprain is obviously of little consequence and there is no point in delaying definitive treatment.

Epiphysial Injury.—Epiphysial injuries are rare but can be alarming, occurring usually at the distal end of the femur and at times presenting such gross deformity as to raise the possibility of injury to the popliteal nerves and blood vessels. The sooner reduction is effected the better. Again, roentgenography is essential.

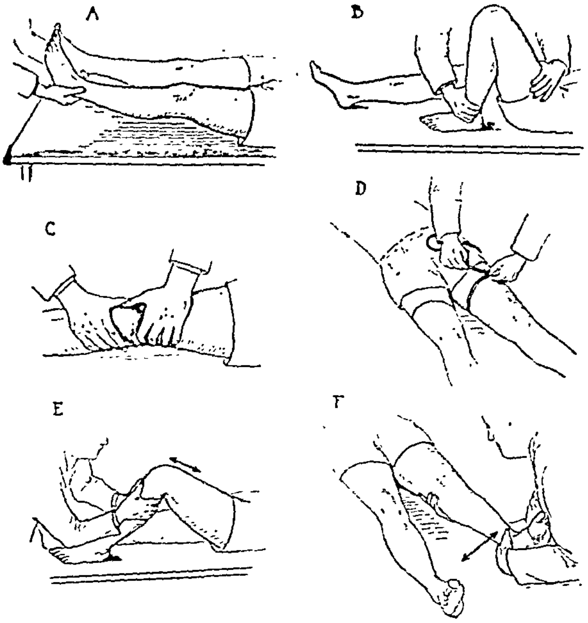

Fig. 1.—Basic steps in examination of knee. Subject is supine and completely relaxed. All steps are first done on uninjured leg. *A*, inspection and determination of extension; *B*, determination of active and passive flexion not carried beyond point of pain; *C*, palpation for fluid—pressure on suprapatellar pouch drives small quanities of fluid downward; right index finger is shown about to compress anterolateral aspect of joint. producing fluid wave palpable by thumbs and left hand; *D*, determination of muscle atrophy—circumference of thighs is measured at same level; *E*, determination of cruciate ligament laxity—knee is flexed at 90 degrees and examiner's forearm presses firmly against lower part of tibia while both hands grasp leg, manipulating it in sagittal plane; *F*, determination of collateral ligament laxity—one of examiner's hands rests on table and grasps femoral condyles, other grasps ankle and manipulates extended knee in coronal plane (reprinted with permission from *Surgery, Gynecology, and Obstetrics* [87:569 (Nov.) 1948]).

Fracture.—Fractures are unusual before the age of 35 years and then occur most frequently in sports involving high speeds and great force, such as skiing. Definitive diagnosis is, of course, made roentgenographically.

Occasionally momentary lateral dislocation of the patella is encountered and can be confusing, presenting symptoms and signs suggesting a combination of contusion and ligament injury. However, dislocation of the patella usually occurs in persons with knock knee deformity, hypermobile patellas, and a history of previous dislocation.

Treatment

The first examination, ideally carried out shortly after the injury, should identify and separate major injuries requiring prompt definitive surgical care in a hospital from minor injuries which can be treated on an ambulatory basis.

Gross epiphysial displacements should be reduced by manipulation, with the patient under anesthesia, and the patient should then be immobilized in a plaster spica for at least eight weeks. Open operation should be undertaken only as a last resort. Fortunately, functional results are good and growth disturbance is unusual, since the injury is primarily one of shearing rather than compression, and the epiphysial plate is not often seriously damaged.

Fractures are treated by closed manipulation, traction, plaster immobilization, and operation, as the characteristics of the particular injury, the patient, and available facilities and skills dictate. The underlying philosophy, as in the treatment of any injury, should be the restoration of as near normal function as possible, in the shortest possible time, with the least risk to life or limb. In children and adolescents (as in patients with epiphysial injuries) open operation should be undertaken only as a last resort.

When the presence of complete ligament rupture has been established there is little reason today to refuse the patient the benefits of prompt surgical repair unless serious contraindications, such as grave concomitant disease, either general or in the extremity, exists. Such contraindications are rare in persons participating in sports. The philosophy of prompt surgical repair rather than immobilization and hope has been well established in the last decade[5] and recently has been supported by the experimental work of Clayton.[6]

The torn meniscus does not heal unless the tear is peripheral between the meniscus and the capsule of the joint. There is no way accurately to determine the position and extent of the tear in a meniscus. Arthrography has not proved universally reliable and if immobilization for several weeks in plaster is carried out on the assumption that the tear is peripheral and the meniscus might heal, atrophy of the thigh musculature inevitably occurs. If operation is later found necessary, as is usually the case, disability imposed by the atrophy is greatly prolonged. Immobilization, therefore, has little place in the treatment of injuries to the meniscus or ligament.

When symptoms and signs are clear after the sprain accompanying most meniscus injuries has healed, operation should be delayed only long enough to teach the patient the patterns of exercise he will do after meniscectomy. The operation should only be an incident in the total management of the injury and the patient. Aspiration may be necessary if the joint becomes distended, but it should not be forgotten that arthrocentesis is, from a bacteriological point of view, no different than arthrotomy and should be carried out with the same sterile precautions. The entire meniscus should be removed and active motion instituted as soon as it is comfortably possible. Exercises should begin the day after operation and should continue with increasing vigor until full function has been regained. Weight-bearing should not be permitted until the soft tissues have healed, no sooner than 10 to 14 days after operation. Full function should be restored 8 to 10 weeks after operation, but heavy contact sport should be forbidden for at least four months. Full normal function should be the rule rather than the exception after prompt ligament repair or meniscectomy. Athletes should be able to return to their sports without disability.

Contusions and ligament sprains constitute minor injuries, unless tissues are ruptured. Their pathology is the same. Immediate hemorrhage is followed by phagocytic infiltration of the hematoma, fibroblast proliferation, and finally scar tissue formation. The object of treatment is to assist nature. This is accomplished by the immediate application of cold, to constrict the arteriolar bed and thus diminish hematoma formation; compression, to disseminate the hematoma and speed its absorption; rest, to allow the process of healing to continue uninterrupted; and elevation, to minimize edema.[7] Twenty-four hours after injury the sources of bleeding can be considered as closed, and heat can be applied to bring more blood to the part and hasten the dispersal of the products of injury.

Application of cold is accomplished by means of an ice pack or cool bath. Compression is created by the appropriate use of foam rubber and elastic cotton bandages. Rest is achieved by the use of crutches. Most athletes are strangers to crutches and must be instructed in their use to avoid injuries to the brachial plexus and blood vessels in the axilla. Use of hot water is as effective a means of applying heat to a contusion or ligament sprain of the knee as any more complex modality. Diathermy, in fact, is contraindicated, since its use is followed by a high incidence of effusion. There is no specific virtue in ultrasound therapy and its employment requires considerable skill.

More important than heat and massage is active exercise within the limits of comfort. Atrophy of the thigh musculature occurs at an astonishingly rapid rate after knee injuries and can be prevented only by a carefully supervised daily pattern of progressive resistance exercise.[2]

Scar tissue is always weaker than the tissue it replaces, and there is thus some basis for the ancient adage, "once a sprain, always a sprain." When full function, including muscle power, has been regained after a ligament sprain of the knee, the ligament should be protected for at least a year from reinjury. The disorderly pattern of inelastic collagen fibers in scar tissue is only very slowly replaced by orderly elastic tissue. The best protection is afforded by adhesive taping of the

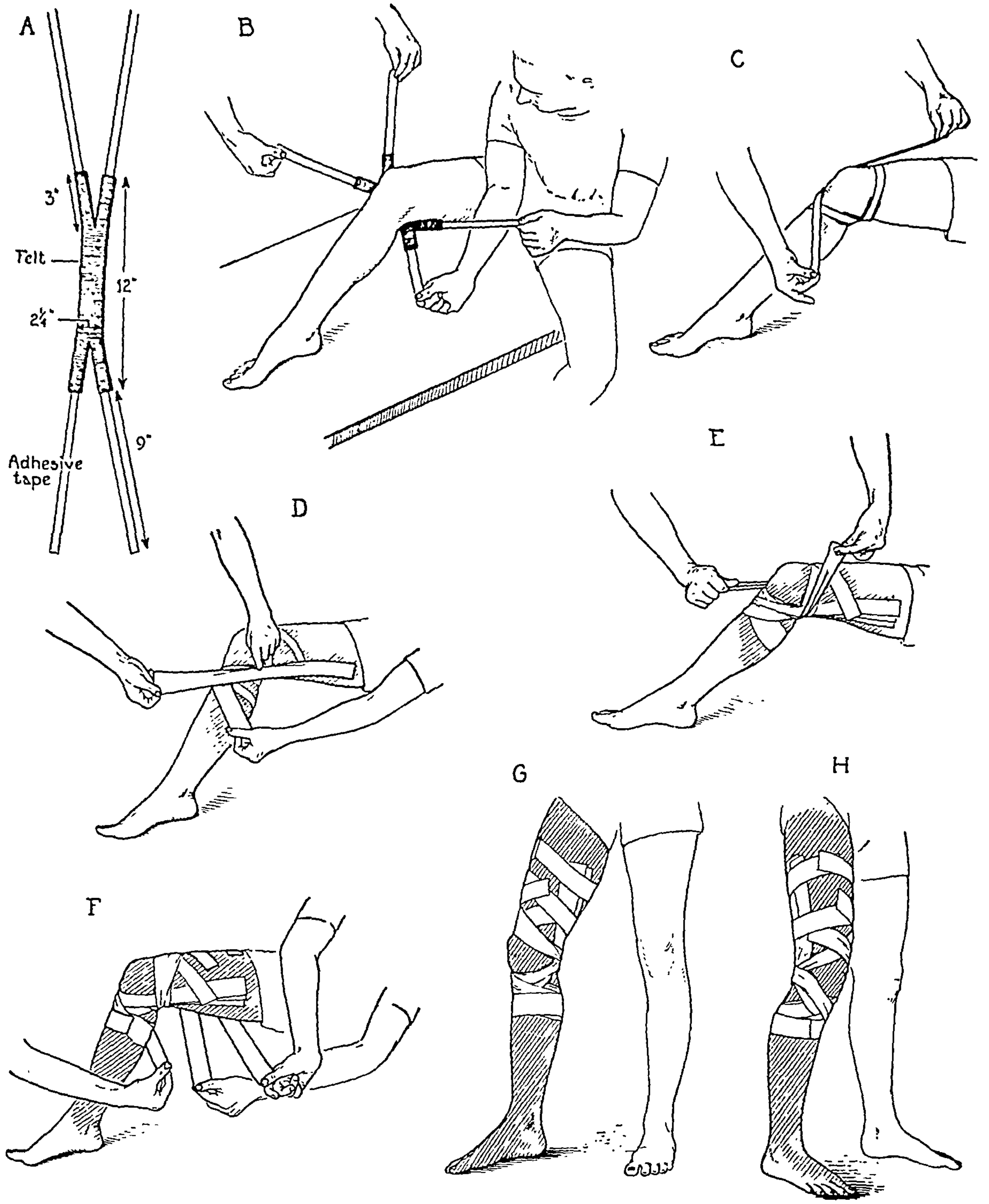

Fig. 2.—"Duke Simpson" protective knee taping. *A*, details of cruciate ligament–supporting component. *B* and *C*, application of cruciate ligament–supporting component. *D*, application of medial and lateral ligament supporting components, three on each side. *E*, reinforcement of cruciate ligament–supporting component. Two strips of tape are applied, crossing anteriorly above and below joint. *F*, application of circular anchoring tapes. *G* and *H*, completed taping (reprinted with permission from *Surgery, Gynecology, and Obstetrics* [87:569 (Nov.) 1948]).

"Duke Simpson" pattern (fig. 2).[8] This reinforces both collateral and cruciate ligament systems and is effective for several hours after its application. Most steel and leather knee supports are constructed on the basis of the false assumption that the knee is a simple hinge. To be effective they must be molded carefully to the midcalf and thigh and have a double toggle joint at the knee. They are thus expensive and impractical for ordinary use. Short elastic sleeves with small, hinged steel supports on the medial and lateral sides are useless.

319 Longwood Ave. (15).

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ATHLETIC TRAINING, PROTECTIVE EQUIPMENT, AND PROTECTIVE SUPPORT

Kenneth B. Rawlinson, Norman, Okla.

Three important elements in a program for preventing athletic injuries are thorough physical examination, maintenance of good practice conditions, including practice field and practice equipment, and careful mental and physical conditioning of the players. The physician who is really in touch with trainers and athletes can help greatly with advice on special problems of prevention of injury as well as rehabilitation of the injured. New materials have become available for use in protecting vulnerable parts against strains and blows. Because of the frequency of certain types of injury, football and basketball players should have their ankles either taped or wrapped before each practice session. The methods here described for supporting the ankle and the longitudinal arch of the foot have been used routinely at practice sessions for many years and are believed to have prevented or to have reduced the severity of many ankle injuries.

An athletic trainer's duties can be placed in three categories: (1) prevention of injuries, (2) treatment of injuries, and (3) rehabilitation of the injury and the athlete as a whole. I would like to discuss duties in each of these fields.

Prevention of Injuries

It is our duty to stress prevention rather than care of injuries. We spend much more time on prevention than the average layman believes. We work on the assumption that the more injuries that can be prevented the fewer patients will have to be treated and rehabilitated. Since an injured athlete is of no value to his team, his coach, or himself, from an athletic standpoint, the greatest concern must be with prevention of the injury which causes him disability.

Many factors go into the field of prevention. As a part of prevention no person should be permitted to practice or participate in any sport until he has

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Assistant Professor of Physical Education and Head Athletic Trainer, University of Oklahoma.

Read in the Symposium on Athletic Injuries before the Joint Meeting of the Section on General Practice, the Section on Orthopedic Surgery, and the Section on Physical Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959. The paper read in the panel discussion on protective equipment and support has been incorporated, with the author's permission, in his paper on athletic training.

successfully passed a thorough physical examination. At the University of Oklahoma we give our physical examinations on the so-called assembly line technique. Our team physician, doctors from the health service, and nurses give physical examinations at the student infirmary at 8 a. m. on the day before fall practice starts. Each doctor takes a station. The boys are given their record cards and they merely go from station to station. With use of this technique we have been able to give our varsity football squad their physical examinations in about one and one-half hours.

I would recommend that a physician be on the bench at every contest. It may be necessary, in some localities, for various doctors to take turns; but, regardless of how it is done, you can be rendering a service to your community by donating your services for a couple of evenings each year.

A second phase of prevention is the maintenance of a good practice field. Many schools spend most of their money and all of their time maintaining a so-called perfect game field—a field the spectators will see and the team will use four or five times a year. I would recommend that this procedure be reversed and that the practice field, which is used as much in a week as the game field is in a season, be kept in A-1 condition at all times.

Another phase of prevention is the physical and mental conditioning of the squad. At the University of Oklahoma this is an important part of our total program. No team is any better than the physical condition of its players. Red Sanders, the late head football coach of the University of California at Los Angeles, once made the statement that football is 40% ability and 60% physical condition and mental attitude. Tom Harmon, former Michigan All-American player, stated that football these days is 90% mental and physical preparation. It all boils down to the axiom that no team is better than its physical condition. Our objective is to get the team, as a whole and as individuals, physically stronger and tougher than the opponents.

Good equipment is an important factor in the prevention of injuries. Some schools make the same mistake with equipment as they do with their practice fields. They spend the greater portion of their budget for some gaudy, fancy game suit that is only going to be worn 8 to 10 times a year. I believe that a school should spend most of its money for the equipment that is worn daily—practice equipment. Of all the equipment worn by a football player the most important is the headgear. Other important pieces of equipment are the shoulder pads, shoes (well-fitting and not necessarily the most expensive), and pants that fit the player.

From time to time during the season, it is necessary to improvise or purchase special equipment to protect a special injury. A fracture glove may be necessary to protect a hand injury, a pair of "Big Boy" shoulder pads to protect a bruised shoulder, or a pair of "Peel Blocker" hip pads to protect an iliac crest. It may be necessary to build up a pair of regular shoulder pads with sponge rubber or plastic or to use a folded towel around the neck to prevent recurring neck sprains or nerve contusions.

It is necessary, in fielding a team, to do a considerable amount of preventive and protective taping. At the University of Oklahoma every member of the football and basketball squads must have his ankles either taped or wrapped before each practice session or game. An ounce of prevention is worth a pound of cure.

Protective Equipment and Protective Support.—Equipment is much better today than it was 30 years ago. However, there is still room for improvement. Thanks to the manufacturers we are getting better equipment every year. The old type of headgear has given way to the new suspension type or a plastic molding in place of the old sponge rubber. Shoulder pads can now be purchased in four standard types of construction—flat, inside cantilever, outside cantilever, or double cantilever. In addition, there are special shoulder pads, such as the Big Boy, which remove most of the pressure from the shoulder and diffuse it around the rib cage.

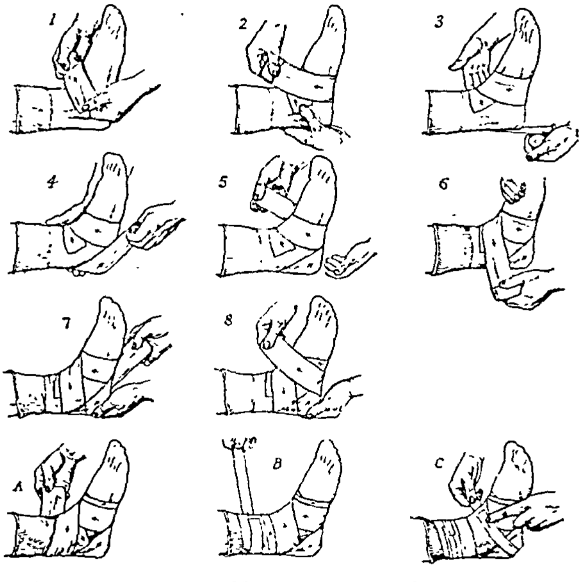

Fig. 1.—Louisiana ankle wrap. 1-8, application; 3-8 may be repeated to provide two lifts on each side of heel. (*A*) wrap is spiraled up over ankle. Two pieces of tape are used to secure wrap, one around top (*B*), and one across heel (*C*). Single lift is demonstrated. For 72-in. wrap, spiral up ankle as shown in *A*, *B*, and *C*. For 96-in. wrap, repeat 3-8 for two heel lifts and then spiral up ankle.

Another great improvement has been in the field of padding or cushioning of the equipment. In past years this was all done with sponge rubber, felt, or kapok. Today most pads are covered with a plastic material known as Absorblo or Ensilite.

This material will absorb much more shock and is also more sanitary, since it will not absorb moisture and can be readily cleaned with soap and water.

As the styles and types of equipment have improved, the weight of the uniform used by players today has decreased. I have no specific figure on the weight of the uniform of the past generation, but I imagine it was between 20 and 25 lb. In comparison, the uniform one of our halfbacks wore in last January's Orange Bowl game weighed 12 lb. 2 oz.

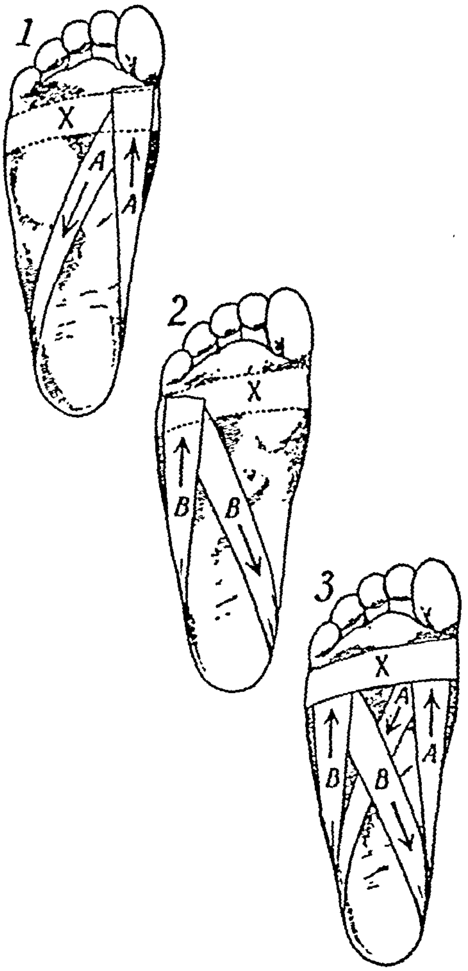

Fig. 2.—Longitudinal arch strapping.

I would like to describe some of the methods of prevention and protective strapping used at the University of Oklahoma. All of our ankle wraps are placed on the ankle over one pair of athletic socks, to prevent friction, blisters, and possible undue constriction. When we use adhesive tape, we almost always apply the tape directly to the skin. Naturally, we prepare the skin first by shaving off the hair and applying a benzoin balsam aerosol (Tuf Skin) or quick-drying adherent before applying the tape. The methods of taping are the (1) figure-eight ankle wrap, now obsolete; (2) Louisiana ankle wrap, preferred (fig. 1); and (3) adhesive tape basket-weave with Oklahoma heel lift, with or without the felt "U." I use the Louisiana ankle wrap or the adhesive basket-weave on all of our athletes. I believe that this has prevented or reduced the severity of many ankle injuries. In a survey made at Harvard University, Quigley and co-workers[1] stated that in the 15 years since they had started the routine use of ankle wraps none of their athletes had suffered a complete ankle ligament rupture. Dr. D. F. Hanley of Bowdoin College phrased it a little differently when he said, "We have not lost a man for a game in five years who has worn his ankle wraps correctly." Other forms of strapping that are used at the University of Oklahoma include longitudinal arch strapping (fig. 2), footrest strapping, and knee strapping, including methods of supporting the medial, lateral, and cruciate ligaments and of supporting injured knees postoperatively.

Treatment of Injuries

Treatment of injuries is actually a minor part of our job. We are the coordinators between the coach and the physician. In reality, we are the "suspecticians" and physicians are the diagnosticians.

Rehabilitation

As in the treatment of injuries, in rehabilitation the trainer works hand in hand with the team physician. Rehabilitative exercises should be started as soon as possible after an injury. In fact, it is advisable to continue exercising other portions of the body even though the injured part must of necessity be immobilized. It is much better to prevent atrophy than it is to relieve it. Summarizing our work in the fields of treatment and rehabilitation, we work together with our team physicians with the same set of rules, the same set of signals, and the same objective—the complete rehabilitation of the athlete.

I have been asked about the injury problems seen in college that could have been taken care of in high school. At present, high school injuries which give the most trouble are injuries to the knee, myositis ossificans of the humerus, and a few shoulder and ankle injuries. Regardless of the injury, I would recommend early rehabilitation or early surgery and rehabilitation. Be fair to the boy. If he needs surgery in high school, recommend it. Don't wait until he gets to college, where he will be a disappointed athlete.

In conclusion, on behalf of all trainers, I want you to know that any help the medical profession gives to us is and will be greatly appreciated.

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BRIEF MAXIMAL ISOTONIC EXERCISES IN THE TREATMENT OF KNEE INJURIES

Donald L. Rose, M.D., Kansas City, Kan.

The clinical value of a specific technique of exercise was investigated in 47 adults with unilateral injuries to the knee. The patient, in the sitting position, used the quadriceps femoris to extend the knee against a maximum weight load and to maintain full extension for five seconds. This was done once daily. The load was increased by 1.25 lb. (0.63 kg.) each day. The strength of the uninvolved leg was determined not oftener than once weekly. Three case histories illustrate the sequence of events. Under these conditions the prescribed exercise produced a steady increase in strength of the ipsilateral muscle up to a maximum, with corresponding resolution of clinical symptoms; no crossing of strength effect between the ipsilateral and contralateral muscles was observed.

Injuries to the knee structures occur frequently, during a variety of athletic activities. The mechanism of injury, regardless of the precipitating circumstance, is simply one of the application of a force greater than that which normally stabilizes the joint and which is applied in a direction different from that of the stabilizing forces. Although the injury usually organically damages the extramuscular structures, the musculature itself is invariably involved in the development of weakness, atrophy, tremor, pain, discomfort, apprehension, a feeling of insecurity, or a lack of confidence in the part on attempted function. These symptoms begin immediately after injury and not until they are resolved does clinical recovery result. The purposes of this paper are to discuss an apparently effective means of controlling these obvious functional abnormalities which are associated with the injury and to call attention to the importance of an adequate neurological component of neuromuscular activity.

Without real evidence for its substantiation, the belief has existed that muscles must be repetitively "loaded," if maximal strength is to be obtained. The work of Hettinger and Müller [1] was the first to delineate certain of the dosage elements of therapeutic exercise. These authors concluded that the greatest increase in strength occurred when the muscle was loaded to a point near its maximum, that one exercise period per day was as effective as multiple periods, and that one six-second contraction sustained isometrically was as effective as one of a longer period in the induction of strength. These results have been confirmed by others, who have used both isometric [2] and isotonic [3] exercises. Inasmuch as these studies have indicated increase in strength with single effort, it would seem clear that the traditional concept of strength (its being equivalent to the physical formula for work) should be reexamined.

Technique

The technique of loading the quadriceps femoris after the manner popularized by DeLorme [4] was used. It should be emphasized, however, that the intent of the exercise procedure was to develop a technique whereby the phasic movement pattern could be maintained against successively increased mechanical stress, which would, therefore, increase the functional capacity of the pattern. This differs fundamentally from isometric exercises, which prohibit the achievement of movement and which may fail to produce the elements necessary for the synthesis of phasic movement patterns.

The exercise bout in its entirety was as follows: After proper positioning of the subject and attachment of the weight load to the foot, the leg was extended from a position of 90-degree flexion to maximal extension and maintained in maximal extension for five seconds by timed count. The initial position was then resumed and the weight was removed.

The initial weight lifted was the maximum amount, as determined by only two or three attempts. This small number of initial attempts is to be emphasized, not only for the purpose of determining the approximate maximal capacity of the neuromuscular effort but, above all, to minimize the cumulative inhibitory influence of painful proprioceptive feedback on the movement pattern.

On the next attempt a given weight was added to the amount previously lifted. This added weight was termed the increment unit. On each successive occasion thereafter the increment unit was added to the amount of the immediately preceding lift. The size of the increment unit was important. It has previously been reported [3] that an increment unit greater than 1.25 lb. (0.63 kg.) was too great

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From the Department of Physical Medicine, University of Kansas Medical Center.

Read in the Symposium on Athletic Injuries before the Joint Meeting of the Section on General Practice, the Section on Orthopedic Surgery, and the Section on Physical Medicine at the 108th Annual Meeting of the American Medical Association, Atlantic City, June 12, 1959.

for this particular muscle. This sequence was repeated, and an attempt made to add an additional 1.25 lb. each time until the ceiling of strength was attained. Maintenance of this ceiling maximum was achieved by periodic lifting of this weight once weekly or less often. The effect of cross-education [5] was determined by measuring the maximal strength of the unexercised leg occasionally but not oftener than once weekly.

The effect of the exercise procedure on muscle hypertrophy was determined indirectly by measuring the circumferential diameter of the thigh by means of steel tapes 4 and 8 in. (10.2 and 20.3 cm.) above the superior pole of the patella. Such measurements were recorded with the subject in the standing position, with the quadriceps contracted.

The exercise principle and procedure were explained to the patient initially. So far as the weight lift was concerned, no systematic attempt was made to conceal or to reveal its amount. The subject usually inquired after the lift attempt and was told the amount. Although the value of external stimulation on motor performance is recognized, for the purposes of this study it was preferred that such performance be the result of internal stimulation and motivation insofar as possible.

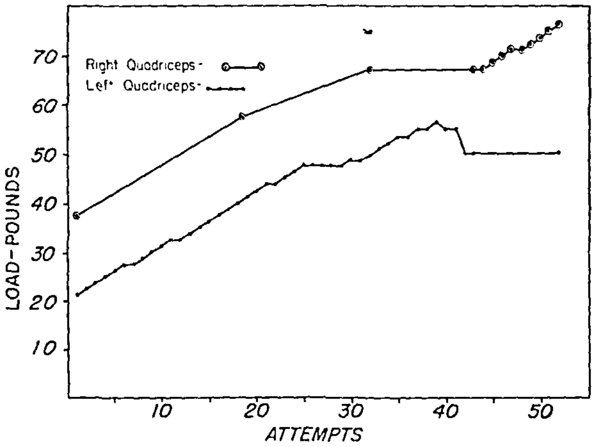

Fig. 1.—Induction of strength after sprain of medial collateral ligament of left knee. Exercise sequence was prolonged beyond clinical recovery.

Material

This study is based on data derived from 47 adults who had sustained unilateral injury to the knee during the course of athletic pursuits. Most of the group (30) were college-age adults; the rest ranged from this age up to that of 64 years. Forty were men. Not all were necessarily injured in competitive sports. The classification of injury was as follows: collateral ligament sprain, 20; traumatic synovitis, 5; postmeniscectomy, 12; and postfracture, 10.

Results

Because the strength of each person is strictly an individual matter, it was impossible to average strength by groups or injury in any meaningful sense. Nevertheless, as a group, the athletes were stronger initially on both normal and injured sides than were those who did not habitually engage in strenuous physical exertion. There was no sex difference in this respect, nor did age apparently make any difference.

The 1.25-lb. increment unit, determined in normal persons [3] as the added amount which could be lifted each time, was equally applicable to the subjects with injury status. Nearly all of the subjects increased the strength of the quadriceps femoris by the increment unit at each exercise effort, as shown in figure 1. In fact, the lack of such regular response invited careful consideration of psychological factors to account for this; among these factors may be mentioned lack of motivation, apprehension, fear of further injury, pain, and malingering. Usually these psychological factors could be resolved by explanation and reassurance.

The upper limit of strength so induced also appeared to be of psychological origin. All subjects, normal [3] or injured, commented that further increase in strength was impossible because of an ill-defined but universally expressed fear of impending damage to the knee structures if an added weight increment should be attempted. This "ceiling" was constant and apparently valid, since it could not be exceeded in a given person even when he did not know that a supramaximal weight lift was being attempted. It is of interest also that the initial maximum could not be exceeded if there was the feeling of impending harm to the knee, were heavier weights to be lifted. With resolution of this attitude, the inhibitory influence was removed and the usual strength induction curve was developed.

With one exception, all patients in this group became asymptomatic after no more than 10 exercise attempts. One subject, initially given the diagnosis of a sprain of the medial collateral ligament, complained of increasing pain with each weight lift. Subsequent arthrotomy disclosed a fracture of the medial meniscus and this section of the cartilage was removed; the postoperative course of exercise in this patient was the same as that in others of the series. The absence of subjective complaints led a number of patients who were college students to discontinue the exercise procedure and to resume their usual athletic pursuits. It is fairly certain that they remained asymptomatic, or they would have been seen in the student health service.

The phenomenon of cross-education was repeatedly demonstrated in this group. In normal persons the strength curve of the unexercised extremity should keep pace with that of the exercised extremity.[3] Attempts were made to utilize this phenomenon in an effort to delay the weakening effect of trauma and enforced inactivity. These results, largely negative, may be summarized by reports of three cases.

Case 1.—A 20-year-old woman suffered a sprain of the medial collateral ligament of the left knee when she collided with other players during a basketball game. Brief maximal isotonic exercise of the left quadriceps was begun on the day after the injury. Figure 1 illustrates the response to such exercise. A cross-education effect on the uninvolved extremity was noted during the forepart of the exercise experiment. However, when the ceiling maximum was reached on the side of injury, daily exercise of and increase in strength in the uninvolved extremity resulted in no apparent further change in strength on the side of injury. In other words, the ceiling maximum is constant and not subject to further change.

Case 2.—A 21-year-old male athlete underwent an arthrotomy for a fractured medial meniscus of the left knee. On the second postoperative day the brief maximal isotonic exercise was begun to the right (uninjured) quadriceps. The graph to the right in figure 2 illustrates the strength findings. When the cast was removed the quadriceps of the involved extremity was quite weak, although the strength of the normal extremity had increased 35% over the initial value. After the initial psychological barriers were overcome, with regard to exercising the involved side, the strength induction curve on this side paralleled the much greater strength curve of the normal extremity. There was, therefore, no evidence of transfer of neuromuscular capacity to the involved extremity during its period of immobilization.

Case 3.—A 19-year-old male athlete sustained an arthrotomy for a fractured medial meniscus of the right knee. Brief maximal isotonic exercise of the left (uninvolved) quadriceps was begun on the third postoperative day. The graph to the left in figure 2 demonstrates the exercise responses in this case. As with the patient in case 2, there was no conclusive evidence that exercise of the uninvolved extremity had any salutory effect on the injured extremity. Further, the subsequent development of pain on effort resulted in prompt additional functional loss of strength which required an additional two-week period of exercise for recovery. It should also be noted that, although the strength of the involved extremity was increasing at the usual rate, there was no evidence of further increase in strength of the normal extremity, which apparently had already reached ceiling maximal strength.

Several incidental observations should be summarized. Tremor was one of the first symptoms to disappear. Although quadriceps atrophy, when present, was rapidly resolved during the exercise period, muscular hypertrophy was never seen clinically; this was true even though some subjects were able to lift the relatively enormous weight of 125 lb. (57 kg.). Each weight lifted taxed the person's strength and determination (at times colored by considerable intrapersonal conflict), yet there was no postexercise sense of fatigue, stiffness, or pain that did not exist prior to each exercise period. Despite the obvious increase in strength, there was no feeling of increased strength, rather only a normal attitude of confidence and security in the part. Finally, each quadriceps seemingly is independent of the other with respect to initial and final strength.

Conclusions

In a series of 47 patients with unilateral injury to the knee the quadriceps femoris was loaded isotonically and maintained at maximal contraction for five seconds. An increment unit of 1.25 lb. (0.63 kg.) was added to the amount of the preceding lift at each successive period. This increment unit appeared to be constant, regardless of the initial strength or weakness of the muscle clinically, and was regarded as neurogenic in origin. The maximal strength so achieved was limited by psychological factors. Use of this method made possible the rapid resolution of subjective symptoms of pain, stiffness, and the feeling of insecurity after a variety of athletic injuries to the knee structures. The phenomenon of cross-education appeared to be of no value clinically.

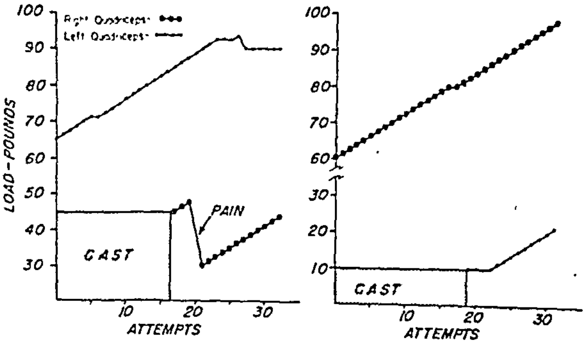

Fig. 2.—Induction of strength after arthrotomy for fractured medial meniscus, showing failure to demonstrate significant cross-education effect. Data are charted by attempts.

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REPORT OF ACTIVITY OF THE AMERICAN MEDICAL ASSOCIATION COMMITTEE ON INJURY IN SPORTS

Allen J. Ryan, M.D., Meriden, Conn.

Physicians in the United States have been active as sportsmen and as medical advisers to athletes since the beginning of organized athletics. Until recently there was no organized approach, however, on the part of medical associations or societies to the problems of sports medicine. This is in distinct contrast to the situation in Europe, where well-defined programs have been in existence for so many years that this branch of medicine has become a specialty in itself.

The original suggestion for the establishment of a Committee on Injury in Sports was made at a meeting of the Board of Trustees of the American Medical Association in December, 1953. Exploratory contacts were made and letters sent to interested physicians, which resulted in the appointment of such a committee under the chairmanship of Dr. Augustus Thorndike of Boston in 1954. The first meeting of the Committee took place in Chicago in June, 1956. Since that time the Committee has met regularly twice a year, in different parts of the United States, and has undergone a few changes in its membership. Fred Hein, Ph.D., of the Bureau of Health Education, has served as secretary to the Committee.

Considerable thought and discussion were devoted, prior and subsequent to the first meeting, to the nature of the role which this Committee should play. Would it be a passive spectator of events in the field, noting progress and problems and answering requests, or should it take an active part in making inquiries itself, setting standards and shaping events in the process of its activities? The decision was gradually reached to become active. Since then, the press of developments has resulted in constant year-round activity conducted through the staff secretary and the Chairman by correspondence with the Committee members between meetings.

Although it is perhaps a little premature to speak about accomplishments in a field in which so much remains to be done, the scope of the problems with which the Committee is dealing may best be understood by considering what has been done and what is in progress. Most important of all, in whatever has been attempted so far, has been the enthusiastic response and excellent cooperation received from representatives of the sports world, both amateur and professional, educational institutions, and the members of the medical profession as a whole by this Committee.

One of the first problems which came to the attention of this Committee was that of the apparently increasing number of serious and even fatal head injuries occurring in football players. Contact was made with a research program on the subject of protective headgear for all purposes being carried out at Cornell University under the direction of George Dye, Ph.D. Discussion with representatives of the larger manufacturers of football headgear followed, and subsequently a visit was made to the laboratory of sports medicine at Michigan State University where headgear research was being carried out under the direction of Henry Montoye, Ph.D. Progress has been made, not as the result of this Committee's efforts, let it be said, but with its active encouragement, in the production of a new, safer type of football helmet. It is hoped for the future that a set of test standards will be arrived at to serve as guides for the manufacture of even safer helmets. In the meantime, the Committee is emphasizing to those concerned the importance of buying the best head protection available and of cultivating serious respect for any type of head injury occurring in practice or game and in the treatment and aftercare thereof.

This approach to this particular problem inaugurated the practice of making one meeting each year a visit to one of the university centers where active programs of research into the physiology of sports activities are being conducted. In 1958 the Committee visited Springfield University, where the program was arranged by Dr. Peter Karpovich in his laboratory. The Committee hopes not only to keep informed of what is happening in such programs but to encourage the development of new programs, where appropriate facilities and qualified personnel exist.

As the scope of its inquiries widened, the Committee made contacts with the National Collegiate Athletic Association (NCAA), the National Association of Intercollegiate Athletic Associations (NAIAA), and the National Federation of High School Athletic Associations (NFHSAA). These contacts have been most rewarding, and they are all bearing fruit.

In the first instance, NCAA appointed a special committee of its own on sports injuries and included the Chairman of the A. M. A. Committee as one of its members. This committee has been very active since its inception in planning and conducting a national survey of football injuries and another of training-room facilities. It is currently embarking on a cooperative study of training methods with the American Olympic Committee. It has cooper-

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ated with the A. M. A. in a survey of amphetamine usage among athletes and in the dissemination of the "Bill of Rights for College Athletes" to all of its member colleges. In these two latter projects the NAIAA has likewise cooperated.

The "Bill of Rights for College Athletes" was developed by the Committee from an idea suggested by one of its members, Dr. Thomas B. Quigley of Boston. It is reproduced here in its entirety because it represents the Committee's philosophy of correct conditions for participation in amateur athletic events.

Bill of Rights for the College Athlete

Participation in college athletics is a privilege involving both responsibilities and rights. The athlete has the responsibility to play fair, to give his best, to keep in training, and to conduct himself with credit to his sport and his school. In turn he has the right to optimal protection against injury as this may be assured through good technical instruction, proper regulation and conditions of play, and adequate health supervision.

Good Coaching.—The importance of good coaching in protecting the health and safety of athletes cannot be minimized. Technical instruction leading to skillful performance is a significant factor in lowering the incidence and decreasing the severity of injuries. Also, good coaching includes the discouragement of tactics, outside either the rules or the spirit of the rules, which may increase the hazard and thus the incidence of injuries.

Good Officiating.—The rules and regulations governing athletic competition are made to protect players as well as to promote enjoyment of the game. To serve these ends effectively the rules of the game must be thoroughly understood by players as well as coaches and be properly interpreted and enforced by impartial and technically qualified officials.

Good Equipment and Facilities.—There can be no question about the protection afforded by proper equipment and right facilities. Good equipment is now available and is being improved continually; the problem lies in the false economy of the use of cheap, worn, outmoded, or ill-fitting gear. Provision of proper areas for play and their careful maintenance are equally important.

Good Medical Care.—Good medical care for college athletes includes, first, a thorough preseason history and physical examination—many of the sports tragedies which occur each year are due to unrecognized health problems, and medical contraindications to participation in contact sports must be respected; second, a physician present at all contests and readily available during practice sessions—it is unfair to leave to a trainer or coach decisions of whether an athlete should return to play or be removed from the game after injury, and in serious injuries the availability of a physician may make the difference in preventing disability or even death; and third, medical control of the health aspects of athletics—in medical matters, the physician's authority should be absolute and unquestioned. Today's coaches and trainers are happy to leave medical decisions to the medical profession, and they also assist in interpreting this principle to students and the public.

Other Activities

A similar program for high school athletes has been outlined under the title of "Safeguarding the Health of the High School Athlete." This includes a series of proposed standards for safety in competitive athletics. There is also a guidebook for the holding of local, countywide, or statewide conferences on this subject. The NFHSAA has been actively interested in this program and has further cooperated by conducting a sampling survey of health practices connected with athletic participation in its schools. The monthly bulletin of this organization contains a column on health in relation to sports which is prepared under the direction of this Committee. Currently there is under consideration a series of recommendations relating to the participation of students at the junior high school level in organized football contests.

As the result of several inquiries and the specific interest of several members of the Committee, a statement was issued through the *AMA News* and both college athletic associations on the subject of "making weight" for wrestling and boxing events. Abuses of health involved in heroic weight reduction measures followed by strenuous competition have sometimes resulted in serious illness.

One member of the Committee participated in the revision of an important pamphlet published by the Bureau of Health Education, which is now entitled "Exercise and Fitness." This has a broad circulation among persons working in the field of health, physical education, and recreation. Emphasis is placed on the importance of appropriate exercise in producing and maintaining physical fitness.

During the past year the Committee has cooperated with the United States Olympic Committee in making recommendations for medical personnel to serve at the coming winter and summer Olympic Games of 1960. This is the first occasion on which consultation has been sought with official representation of the profession on these selections. It represents an evident desire on the part of all concerned to see that our finest athletes get the best medical care.

In June, 1958, at San Francisco the Committee presented, at the invitation of the Council on Scientific Assembly of the Annual Meeting of the American Medical Association, a symposium on athletic injuries, their prevention and treatment. Guest lecturers covered topics from skiing to skin-diving. The papers were subsequently published in THE

JOURNAL. In June, 1959, the Committee cooperated in the presentation of a similar symposium with the Section on Orthopedics at the annual meeting of the A. M. A. in Atlantic City.

For the future, it is the hope of the Committee that within the scope of the A. M. A. a national organization of physicians interested in the relationship between sports and medicine, whether as team physicians, research investigators, active participants, or merely fans of sport, may be established. To this end it will continue to encourage informal meetings, presentations in connection with established formal meetings and congresses, publication of articles and essays, and active research, wherever these activities may be carried out. In this way there can be developed a program at least comparable and hopefully superior to any existing in other countries today.

147 W. Main St.

CLINICAL NOTES

ALBUMINURIA AND HEMATURIA IN BOXERS

Capt. Frank B. Flood (MC), U. S. Army (Res.)

The literature contains only a few reports concerning albuminuria and hematuria in boxers. The first article, reporting on 103 boxers, appeared in 1954.[1] Since then, only one further study has been made, on a larger series of 764 fighters.[2] A recent Army boxing tournament at Fort Bliss, Texas, afforded the opportunity to study the problem further; the present study is the first report concerning amateur boxers.

Materials and Method

Forty-three paired specimens of urine were obtained from 35 boxers, one before and one immediately after each bout. Five boxers fought two bouts and one participated in three bouts. The urine specimens were tested for blood with the benzidine test and screened for albumin with use of Uristix strips. We used the criteria of Hepler[3] who stated that results of the benzidine test for blood are considered positive only if the urine contains 12 or more erythrocytes per high-power field. Further, all results showing a trace of benzidine were considered to be negative for the purpose of this study, and only 1+ through 4+ readings were considered positive. If the Uristix strip test for albumin showed a positive result, Exton's method[4] with use of sulfosalicylic acid was used as a check. This method verified the Uristix strip test in all cases; all trace readings were considered negative.

The results of these tests are shown in the table. All Army boxers able to provide paired specimens were included in the study, save five with prebout albuminuria. All of these young men, with an average age of 22 years, were considered in good health. All of them had had negative results of urinalysis on entrance into the service, and all had had repeated physical examinations during and preceding the boxing tournaments.

The large percentage of findings of significant albuminuria (10 out of 43 specimens, or 23%) in the prebout tests of the boxing matches under study may have been present as a result of participation in recent bouts prior to the present study. Two boxers showed significant albuminuria (levels of 3+ or 4+) in each of two prebout specimens, respectively, and one showed a level of 4+ in one prebout analysis. If all boxers with urine specimens exhibiting prebout albuminuria are excluded from the study, then albuminuria developed in the second, i. e., the postbout, specimen in only 5 out of 33 (15%) instances. Quantitatively, the average level of all findings of albumin was 2+ for prebout and 3+ for postbout urinalyses.

Follow-up urinalyses one month later showed that all of the participants in this study had normal urine without evidence of albumin or blood.

Comment

Professional boxing has been termed "the nation's most dangerous trade."[5] In addition to the real possibility of brain damage, the question of renal injury has been raised.

Can exercise, with or without direct renal trauma, produce injury to the normal kidney? Strenuous exercise will produce renal ischemia as the renal plasma flow and filtration rate decrease in response to the demands for increased blood by voluntary muscle. Can the then anemic glomerulus leak protein and red blood cells? If, in addition to ischemia, the previously normal kidney is insulted by direct trauma, will urinary abnormalities appear?

From Fort Bliss, Texas, and the Department of Medicine, St. Vincent's Hospital, New York.

Amelar and Solomon[1] first described these urinary abnormalities in a series of professional boxers. They estimated the number of kidney blows and counted the number of rounds, concluding that hematuria and albuminuria were related mainly to the duration of a match. Direct trauma appeared to play a lesser role, in that hematuria and albuminuria progressed in step-like fashion as the number of rounds in the fight increased, irrespective of "kidney punches."[6] They found that only 65% of these boxers exhibited hematuria from rounds 1 to 6 whereas almost 90% showed renal bleeding during rounds 7 to 12. Albuminuria followed a similar pattern. Because of these findings, the authors recommend urinalysis as part of the prefight examination.

Incidence of Albuminuria and Hematuria in Boxers

			No. of Paired Specimens*		
			Present Study, Amateur Boxers	Amelar and Solomon,[1] Professional Boxers	Kleiman,[2]† Professional Boxers
Blood	Pre fight	Positive	0	0	15(0.7%)
		Negative	43	103	2,185
	Post fight	Positive	12(28%)	75(73%)	415(27%)
		Negative	31	28	1,103
Albumin	Pre fight	Positive	0	0	...
		Negative	33‡	103	...
	Post fight	Positive	5(15%)	70(68%)	...
		Negative	28	33	...

*In present study 12 or more erythrocytes per high-power field considered positive; in studies by Amelar and Solomon and by Kleiman 6 or more erythrocytes per high-power field considered positive.

†682 boxers unable to provide postfight urine specimen.

‡10 (23%) paired specimens exhibiting prefight albuminuria excluded.

Kleiman[2] in 1958 studied a larger group of boxers in regard to hematuria. His findings, based on urinalyses and, in 100 instances, intravenous pyelograms, led him to conclude that exercise alone probably will not cause hematuria in the normal kidney. However, there is evidence to suggest that the normal kidney can bleed and leak protein in the absence of detectable renal abnormalities. Cases of hematuria have occurred after nontraumatic exercise[7]; it appears unreasonable to assume that all of these cases were due to preexisting renal abnormality. The question will remain unsolved in the absence of pyelography in a larger series of fighters showing hematuria. It may be noted that Kleiman[2] found bleeding in 415 (27%) out of a total of 1,518 urine samples taken from professional boxers after a bout, whereas the present study determined that 12 (28%) of the 43 urine samples taken from the amateur Army boxers, who had participated in fewer fights, exhibited postbout hematuria.

Summary

Albuminuria occurred in 15% and hematuria in 28% of a small series of amateur boxers who were studied by means of urinalyses prior to and after their respective bouts. A review of the literature shows our findings to be in agreement on the statistical incidence of hematuria in boxers, as obtained in a larger series. On the other hand, the incidence of albuminuria in this study was much lower than in the larger series (15% versus 68%). If the criteria for determination of albuminuria and hematuria were less strict, the incidence would have been much higher.

The question as to whether previously undetected renal abnormality or strenuous exercise, with or without direct renal trauma, causes hematuria and albuminuria remains unsolved. All boxers, amateur and professional alike, should be required to have a urinalysis as part of the routine examination preceding a match.

The opinions and assertions contained herein are those of the author and are not to be construed as official or reflecting the views of the Department of the Army or the Surgeon General.

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RADIOACTIVE IODINE IN MILK.—On the basis of published data on iodine-131 levels in cow's milk during a 16-month period ending September 1958, the thyroid glands of average infants and children in the U.S. are estimated to have experienced over the last few years annual doses of about 0.1 rad to 0.2 rad from the radioiodine in fall-out. These doses are roughly one to two times the annual dose to such organs from natural background radiation. For a number of reasons, individual thyroid dose rates from fall-out are expected to show wide deviations from the average rate.—Abstract: Thyroid Radiation Doses from Fallout, E. B. Lewis, *Proc. Natl. Acad. Sci.* June, 1959, in *Nuclear Science Abstracts*, Sept. 30, 1959.

SPECIAL ARTICLE

PRIMER ON THE RHEUMATIC DISEASES

PART III

Prepared by a Committee of the American Rheumatism Association

Arthritis due to Infection

Any articulation, spinal or peripheral, may become the site of a septic process, the organism being introduced into the joint directly, by penetrating trauma or surgical procedures, or indirectly, through hematogenous spread from foci elsewhere in the body. Such blood stream seeding may be directly into synovial tissues or may enter the joint secondarily after infection of the adjacent bone marrow. In infants and children, prior to the closure of the epiphyses, the metaphyses are commonly the primary locus of hematogenous dissemination. Although many infectious agents have been found responsible for infected joints, certain ones are so rare as to be of investigative interest only. The more common infecting organisms may be divided into two groups, those causing an acute fulminating type of infection and those engendering a low-grade chronic infection.

Acute Infectious Arthritis (Acute Pyogenic or Septic Arthritis)

This form of arthritis is usually caused by one of the pyogenic cocci, gonococcus, meningococcus, pneumococcus, staphylococcus, or streptococcus. Because of the widespread use of antibacterial agents it is less common now than formerly. On the other hand, the following types of acute infectious arthritis have recently attracted attention, either because of an increased frequency or because of their difficulty in management: (1) that seen in premature infants, (2) that due to resistant strains of staphylococci, (3) that resulting from intra-articular injections or aspirations, and (4) that accompanying malignant disease complicated by infections with enteric organisms.

Pathology.—The inflammatory reaction varies in character and severity with the nature of the organism, state of the host, and duration of the infection. In the more severe suppurative infections rapid lysis of the articular cartilage takes place, particularly at contact sites. Edema fluid and polymorphonuclear leukocytic exudate from synovial granulation tissue give rise to early effusion into the joint. Abscess formation in the synovial and subchondral tissues is frequently present, and massive destruction of the joint tissues may occur. As the infection subsides, fibrous repair of the destroyed articular and synovial surfaces leads to ankylosis.

Symptoms.—Acute infectious arthritis is usually monarticular. Symptoms of an acute inflammatory reaction come on abruptly and develop rapidly. The affected joint is red, hot, swollen, and exquisitely tender. Motion accentuates the pain and, if one of the articulations of the lower extremity is involved, weight-bearing on that extremity is impossible. If the arthritis has developed from a hematogenous spread, a second or even multiple joints may later be involved. Involvement of the spinal articulations is uncommon. Concurrent systemic symptoms of fever, chills, sweats, malaise, and anorexia may occur. These are usually not severe but at times may be sufficient to overshadow the articular involvement.

Laboratory Observations.—Elevated erythrocyte sedimentation rate and leukocytosis, with a rise in the percentage of polymorphonuclear cells, occur early in the condition. The synovial fluid is cloudy or frankly purulent, and the leukocytes may number more than 100,000 per cubic millimeter, with 90% or more polymorphonuclear cells. The organism causing the arthritis can usually be demonstrated by bacteriological studies (both smear and culture) of the aspirated synovial fluid and frequently may also be obtained from the blood.

Roentgenographic Findings.—Roentgenologically visible changes usually occur earlier in acute septic arthritis than in the more chronic varieties. Osteoporosis may be seen within a week and is sometimes visible as soon as the patient reports for examination. If the disease remains untreated, evidence of cartilaginous destruction in the form of narrowed joint space may appear within two weeks, to be followed by osteomyelitis, periostitis, and epiphysitis.

Diagnosis.—The rapidly developing red, hot, swollen, painful, and tender joint of suppurative arthritis may be confused with gout, acute calcific

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The first and second installments of this primer appeared in the Oct. 31 and Nov. 7 issues.

The Committee of the American Rheumatism Association consists of Drs. Darrell C. Crain, Washington, D. C., Chairman; Wallace Epstein, San Francisco; David Howell, Miami; Harry Margolis, Pittsburgh; Elbert Phelps, Washington, D. C.; William Rawls, New York; Edward Rosenberg, Chicago; J. Edwin Seegmiller, Bethesda, Md.; Lawrence Shulman, Baltimore; Leon Sokoloff, Bethesda, Md.; Harry Thompson, Tucson, Ariz.; and Elam Toone, Richmond, Va.

Reprints of the full text of this primer are available from the American Rheumatism Association, 10 Columbus Circle, New York 19. The price per copy is 50 cents.

tendinitis, and occasionally rheumatic fever or rheumatoid arthritis. In the latter two conditions, however, the symptoms are usually polyarticular. Systemic symptoms in gout are usually less severe, and hyperuricemia will be noted. Acute calcific tendinitis presents a characteristic roentgenologic picture. In gonorrheal arthritis the history of an antecedent urethritis may be of assistance. Recovery of organisms from the blood or their demonstration in the joint establishes the diagnosis.

Treatment.—Treatment is directed along two lines: first, to control the systemic and joint infection and, second, to preserve the joint and its function. For the control of sepsis, prompt bacteriological diagnosis with sensitivity studies is essential. Penicillin or one of the broad-spectrum antibiotics will usually be found effective. Against resistant staphylococci, however, erythromycin, chloramphenicol (Chloromycetin), and kanamycin may be the currently preferred drug, but none is entirely effective and newer agents are being sought. Early and vigorous treatment is indicated. In addition to the systemic treatment local therapy is indicated also. Daily aspiration and irrigation with isotonic sodium chloride solution, followed by instillation of approximately 100,000 units of penicillin, will hasten the resolution of the local infection. Broad-spectrum antibiotics are usually too irritating to be used for intra-articular instillation. Open incision and drainage may be indicated.

Immobilization of the joint by splint or traction, in order to control pain and maintain proper position, should be accomplished as soon as possible. This should be discontinued, however, as soon as the acute process subsides, lest adhesions and ankylosis develop. Judicious physical therapy in the form of warm compresses, gentle massage of the muscles above and below the involved joint, and active motion within the range of the patient's pain tolerance are instituted as early as possible in order to maintain optimum function.

Prognosis.—Prognosis as to life is determined by the nature and severity of the systemic disease. Staphylococcic infections in hospitals have at times proved a particularly difficult problem, but even here the outlook is usually good. The prognosis for complete restoration of joint function depends primarily on the time lapse between the onset of symptoms and the institution of specific therapy. It is usually excellent if adequate therapy can be started within the first week; after the third week it is usually poor. Low-grade infections may be overlooked in infants, and irreparable damage may be done before specific therapy is instituted.

Gonococcic Arthritis

The marked decrease in the incidence of joint disease as a complication of gonorrhea is due to the continued effectiveness of penicillin, which cures 95 to 97% of uncomplicated primary infections of the urethra and the cervix. However, gonorrheal arthritis still occurs frequently enough and its clinical manifestations are sufficiently distinctive to warrant special considerations. After the primary infection a latent period of from 10 to 30 days may elapse before the arthritis develops. The onset is customarily sudden, with temperature elevation, malaise, and a polyarthralgia which may simulate acute rheumatic fever. Within a few days the joint involvement becomes monarticular, with a knee, ankle, or wrist being most often affected. Gonococci can frequently be recovered from the joint fluid but rarely from the blood; serologic tests are unreliable. If results of synovial fluid studies are negative, treatment is justified on a presumptive diagnosis based on a history of urethral discharge followed by characteristic joint involvement. Reiter's syndrome (discussed in the section Miscellaneous Arthritic Conditions) may cause confusion. The recommended treatment is administration of 800,000 to 1 million units of penicillin daily for one week. If the patient is sensitive, or the organism resistant, to penicillin, a broad-spectrum antibiotic or sulfonamides are effective substitutes. Intra-articular injections of penicillin in doses of 100,000 units may be used to supplement the systemic treatment but are rarely necessary.

Chronic Infectious Arthritis

This is the term used to indicate the arthritis produced by certain micro-organisms, which, in contrast to the acute fulminating course just described, is characterized by chronic, slowly developing, but persistent joint disease. The term has nothing to do with rheumatoid arthritis, although it was formerly used as a synonym for that condition. Included in this group are infections due to Mycobacterium tuberculosis, Treponema pallidum, Brucella organisms, enteric organisms, and certain fungi. Although all are usually monarticular, there are certain distinctive characteristics of the various arthritides making up this group. Each will therefore be described as a separate entity.

Arthritis and Spondylitis due to Tuberculosis

Incidence.—Although tuberculosis of bones and joints is declining in the United States, it still develops in approximately 1 to 4% of patients who have other forms of tuberculosis. The bodies of the lower thoracic and upper lumbar vertebrae are the most common sites of tuberculous bone infection. Less frequently involved are the peripheral joints; when these are attacked, the lower limbs are more commonly affected than the upper.

Etiology and Pathogenesis.—Tuberculosis in the United States is caused almost exclusively by the human type of M. tuberculosis, the primary lesion developing in the lung through inhalation. From this focus the bacilli spread to the bronchopulmonary lymph nodes, where, under suitable circumstances, hematogenous dissemination to the spine or peripheral joints results. The primary focus may at times be so obscure that the bone disease appears to be primary. Despite the fact that persons receiving treatment with adrenal steroids over a protracted period must be constantly observed for the possible development of a new tuberculous infection or a reactivation of an old one, no case of tuberculous arthritis arising in this manner has yet been reported.

Pathology.—In the spine the earliest lesion is a small tuberculous focus which develops in the marrow of the vertebral body. As the lesion increases in size and caseation occurs, it is referred to as a "cold abscess." With continued growth the bone loses strength and collapses, permitting spread of the infectious material from the cold abscess along the anterior or posterior longitudinal ligaments, with destruction of intervertebral cartilage and involvement of the vertebrae proximal and distal to the original site. The contents of the tuberculous abscess may then dissect between fascial planes or muscle bundles and form a sinus discharging at a point distant from the seat of the main infection. Arrest of the condition, either spontaneously or with drug therapy, may bring about resolution of the lesion and healing by fibrosis or bony union.

In peripheral joints the subchondral area of bone is the most frequent site of the early manifestations of the disease. There, the tuberculous process undermines the articular cartilage and may eventually separate it, spreading to all articular and periarticular tissues. As the disease progresses, the caseation may completely destroy the joint. Here, too, discharging sinuses may occur, although they are less frequent than in the spine.

Clinical Features.—Tuberculosis of the bones and joints occurs most often in children under 15 years of age, although adults are not immune. It is more often associated with active tuberculosis of the lungs or genitourinary tract than with other foci within the body. A history of trauma preceding the onset of symptoms by six or eight weeks may be elicited in about 50% of cases. Involvement of the spine and peripheral joints concurrently is an extremely rare condition.

Tuberculosis of the Spine (Tuberculous Spondylitis, Pott's Disease).—The area usually affected in tuberculosis of the spine is between the sixth thoracic and the fifth lumbar vertebrae, and multiple vertebral bodies may be involved. Signs and symptoms consist of tenderness and muscle spasm over the affected area, weakness and pain often worse at night, rigidity, abnormalities in gait, and kyphotic deformity. Since the anterior margin of the vertebra is usually eroded first, this may lead to collapse and angulation of the spine which can be so severe as to compress the spinal cord, with resultant paralysis. The "cold abscess" described under Pathology may pursue one of several courses. It may remain local, dissect along fascial planes producing a "psoas abscess," appear externally in the inguinal region, or extend into the spinal canal, compressing the cord and producing a tuberculous meningitis.

Tuberculosis of Peripheral Joints.—In adults, the knees are the most common site of peripheral tuberculous arthritis, while in children under 10 years of age hip involvement predominates. The onset is insidious, usually involving a single joint. Local swelling of the joint is noted, and palpation reveals a peculiar doughy feeling, with warmth but rarely redness; muscle spasm and atrophy are present, and finally limited motion. The course is progressive, but transient spontaneous remissions will occur. Regional lymph nodes (called "scrofulous nodes") are frequently involved, with swelling but minimal tenderness. In children the earliest symptom is a limp, slight in the morning on arising but gradually increasing during the day as activities increase. Later there may be pain in the thigh and knee, muscle atrophy, and finally limitation of motion.

Laboratory Examination.—Tubercle bacilli may be found in the synovial tissue or in exudate from a cold abscess or sinus; they are found less frequently in the synovial fluid. They may be demonstrated by smear but are more often recovered by culture or after inoculation of suitable material into a guinea pig. The total cell count of the synovial fluid may exceed 100,000 per cubic millimeter. Although there may be more lymphocytes and monocytes than in other types of arthritis, the differential blood cell count is not specific. The protein content of the fluid is increased and the sugar decreased. Tuberculosis should therefore be suspected in an effusion of short duration if the synovial fluid analysis reveals a moderately low total white blood cell count, few polymorphonuclear cells, a low sugar level, and a high protein content. Biopsy of the synovial tissue or regional lymph nodes will usually demonstrate tubercles and acid-fast bacilli. In tuberculosis of the hip the deep inguinal lymph nodes are often involved, while tuberculosis of the wrist and hand will usually involve the epitrochlear glands. A positive result of a tuberculin skin test is only suggestive, but a negative reaction is strong evidence against the diagnosis of tuberculous arthritis.

Roentgenologic Examination.—In the peripheral joints the first roentgenologic evidence of tuberculous involvement is osteoporosis, accompanied by periarticular swelling. This is followed by marginal erosion, then thinning and interruption of the articular cartilage. The joint space itself may be preserved until late in the disease. In the advanced stage there is subchondral bone destruction and narrowing of the joint space. Spinal involvement presents evidence of bone erosion within the vertebrae, followed by destruction of the intervertebral cartilage and collapse of the bone, with increasing kyphosis of the spine. The shadow of a large caseous mass is frequently noted.

Course and Prognosis.—The introduction of specific therapy in recent years has led to a considerably improved prognosis. Unfortunately, however, the indolent character of the infection may result in considerable progress of the disease before the diagnosis is established. Unless checked, tuberculous arthritis follows a protracted course, leading to progressive destruction of bone and articular structures and not infrequently to disseminated disease. While spontaneous remissions and exacerbations are common, recovery of full joint function is rare. Tuberculosis of the spine carries a decidedly graver prognosis, because of its ability to produce spinal cord compression with paralysis or meningitis. As in other forms of tuberculosis, amyloidosis may be an end-result.

Treatment.—General principles of treatment of tuberculous arthritis consist of (1) the use of antibiotics and chemotherapeutic agents, (2) immobilization of the joint in a comfortable position, (3) prolonged rest and supportive measures, and (4) surgery when indicated. In order to carry out the treatment program effectively the combined efforts of the rheumatologist, internist, and orthopedist are necessary.

Specific antituberculosis drugs are indicated in every case of tuberculous arthritis and spondylitis. Streptomycin, combined with either para-aminosalicylic acid or isoniazid, or both, may be the sole treatment in some cases, but more often these are necessary as adjuncts to surgery. Drug therapy must be continued for a minimum period of six months, with one year closer to the ideal. The usual dose of streptomycin is 3 to 5 Gm. weekly by intramuscular injection, while 12 Gm. of para-aminosalicylic acid is usually given orally each day. Isoniazid is given in an oral dose of 300 to 500 mg. daily.

Surgery may take the form of incision and drainage of tuberculous abscesses; total or partial synovectomy, with the removal of debris from the joint area; joint fusion; or even amputation. Operation of some type is necessary in almost every adult patient with tuberculous arthritis, but children may be treated successfully by means of immobilization, antituberculosis drugs, rest, and supportive measures. The decisions of whether or not operative intervention is indicated and the exact surgical procedure to be employed are primarily orthopedic responsibilities.

Syphilitic Arthritis

The incidence of syphilitic joint disease has been declining steadily because of intensive educational programs and more effective therapy of early syphilis. When it does occur it is usually a manifestation of congenital syphilis or of neurovascular tertiary syphilis. Direct invasion of the joint itself by T. pallidum is virtually unknown.

Congenital syphilis may be manifested in the joints in one of the two following ways. 1. Acute epiphysitis or osteochondritis usually occurs in the first three weeks of life, affects the upper end of the humerus most commonly, and results in flaccidity of the arm (Parrot's pseudoparalysis). It is characterized by inflammatory changes and resulting irregularity of the epiphysial line and periostitis. 2. "Clutton's joints" is a painless bilateral synovitis of the knee developing in children between the ages of 8 and 16 years. Acquired syphilis may, infrequently, during the secondary stage, mimic rheumatic fever or rheumatoid arthritis in the production of arthralgia, synovitis, hydrarthrosis, and tenosynovitis.

The most common form of syphilitic arthritis (which still makes up only a small percentage of the total cases seen in any rheumatology clinic) is that found in conjunction with tertiary syphilis and called "Charcot's joint." In this condition the joint changes are secondary to the spinal cord involvement of tabes dorsalis. Occurring usually in the joints of the lower extremity, this type of arthritis is characterized by gradual painless enlargement, usually of a single joint. The soft spongy enlargement may reach tremendous size, in which case prominent deformity occurs. Not only pain but other sensation may be lost. Roentgenography will demonstrate complete dissolution of the joint and marked remolding of the adjacent bone surfaces. (This entity is discussed more fully under Neurogenic Arthropathy in the section on Miscellaneous Arthritic Conditions.)

Diagnosis.—The diagnosis of syphilitic arthritis is made primarily on the basis of the characteristic clinical pattern, supported by other stigmata of syphilitic infection, plus positive serologic or spinal fluid findings. The laboratory data, while helpful, cannot be used as the sole criterion, since false-positive and false-negative results occur.

Treatment.—Although "Charcot's joint" will not be benefited, other forms of syphilitic bone and joint disease should be treated with standard antisyphilitic therapy. Penicillin remains the preferred drug. The usual course of treatment consists of administration of 6 million units of a depot type of penicillin over a 10-day period. On occasion it may need to be repeated.

Brucellosis

Incidence.—The incidence of brucellosis, like that of many other infectious diseases, is apparently declining, due more to intensive control measures of the reservoir hosts than to currently available therapeutic measures, which are still quite imperfect. Arthritis complicating brucellosis is now felt to be a rather rare condition. Although Brucella melitensis is the organism most likely to produce bone and joint infection, it accounts for only about 10% of generalized brucellosis in the United States.

Symptoms.—Spondylitis is an occasional late manifestation of brucellosis. The symptoms, signs, and roentgenologic changes are similar to those of tuberculosis, except that paravertebral abscesses with sinus drainage are less frequent. The lower thoracic and upper lumbar vertebrae are most often affected, and destruction of the body of the vertebrae, as well as of the intervertebral disk, may occur. Generalized, and often severe, muscle and joint aches and pains, usually diagnosed as fibrositis, may occur during the acute or chronic stage. True synovitis is rare.

Diagnosis.—The diagnosis of brucellosis in general, and of arthritis or fibrositis secondary to it, is fraught with difficulty. A positive blood culture is the main diagnostic evidence that the disease exists, but frequently this cannot be obtained. An agglutination titer of 1:320 or greater in the presence of symptoms of the disease is usually considered diagnostic, although this, too, is open to question. The opsonocytophagic index and the skin test result are not reliable.

Treatment.—The most widely used treatment at the present time consists of the concurrent administration of either chlortetracycline (Aureomycin) or oxytetracycline (Terramycin) orally, with streptomycin given intramuscularly. The dose of the former is usually 0.5 Gm. four times daily and of the latter 1 Gm. per day. The course of treatment must be continued for at least 21 days. It is not always effective, and other wide-spectrum antibiotics are being investigated.

Arthritis due to Mycotic Infections

Coccidioidomycosis.—Coccidioidomycosis is endemic in the southwestern part of the United States but, as a result of modern transportation, patients with the disease are being seen with increasing frequency in many other localities. The causative agent is the Coccidioides immitis, which gains entrance to the body through the respiratory tract. The disease takes one of two forms, that of a benign pulmonary infection or that of a chronic progressive systemic infection.

Symptoms: Muscle and joint pains, often associated with erythema nodosum and called "desert rheumatism," occur in about one-third of pulmonary cases. Affected joints are painful, tender, slightly swollen, but without effusion. This subsides completely within six weeks. At a later date persistent arthritis may develop, frequently at the site of trauma. The infected joint becomes swollen with increased synovial fluid, is moderately painful and tender, and, when in the lower extremity, is the seat of pain on weight-bearing. Such a low-grade monarticular arthritis may persist for years. Destructive lesions may also occur in epiphysial bone.

Diagnosis: The coccidioidin skin test result usually becomes positive after the primary infection but is frequently negative with the disseminated disease. A positive result of the complement-fixation test indicates dissemination of the disease. Diagnosis of the systemic disease is established by demonstration of the organism in sputum, pus, pleural or spinal fluid, or gastric washings, while etiology of the arthritis is best proved by synovial biopsy.

Treatment: Administration of amphotericin B is currently used, although results are not uniformly satisfactory.

Actinomycosis.—Actinomyces bovis affects primarily the mandible but may also affect the thoracic spine. It produces many small abscess cavities in the spine and may be mistaken for tuberculosis of the spine. Administration of large daily doses of penicillin (6 to 12 million units) combined with surgical drainage of sinus tracts and abscesses has constituted the most successful treatment.

Other pathogenic fungi, including Blastomycosis dermatitidis, Cryptococcus neoformans, and Histoplasma capsulatum may, rarely, produce bone or joint disease.

Arthritis due to Virus Infection

In a few instances transient arthritis affecting peripheral joints may be related to viral disease and may be seen in cases of mumps, influenza, and epidemic hepatitis and after smallpox vaccinations. A self-limited arthritis, lasting for about 10 days and involving primarily the small and medium-sized joints, may accompany rubella. A chronic monarthritis or polyarthritis may accompany venereal lymphogranuloma (lymphopathia venereum). There is usually no destruction of cartilage or bone. The result of the Frei test is positive in most cases and affords, with serologic tests, the best means of diagnosis.

Miscellaneous Arthritic Conditions

Although rheumatic fever, rheumatoid arthritis, osteoarthritis, and gout make up the majority of cases of true arthritis seen in any rheumatology clinic, there are other, less common, diseases in which articular structures are involved. Since they frequently present symptoms similar to the four major types, a clear understanding of these conditions is necessary for adequate differential diagnosis. A brief discussion of each is therefore included in this primer.

Reiter's Syndrome

Reiter's syndrome is characterized by the triad of arthritis, urethritis, and conjunctivitis. Many cases will also be accompanied by a dermatitis, involving particularly the hands or feet and resembling keratodermia blennorrhagica or pustular psoriasis. Adult males are mainly affected.

The etiology of the disease is unknown. Although pleuropneumonia-like organisms (PPLO) have been cultured from the urethral discharge in some cases, they cannot be found in most, and, on the other hand, may be found in the urethras of persons showing no evidence of the disease. Viral infections, although often suspected, have never been proved to be related to the condition.

Although symptoms in any of the three major systems listed may precede the others, the full triad is usually developed within 10 to 14 days after the onset. Monarticular arthritis occasionally occurs, but an asymmetrical polyarthritis with a predilection for the knees and ankles is most frequent. Periostitis, especially of the tendo calcaneus, giving rise to heel tenderness, is common. The urethritis commonly appears with a persistent thin, watery discharge. A concurrent gonorrheal urethritis may cause confusion. This, however, is usually thick and purulent and responds to penicillin therapy, leaving the thinner persistent mucoid discharge of Reiter's syndrome. The conjunctivitis varies in intensity from a mild painless reddening to intense involvement complicated by iritis and occasionally corneal ulceration. The disease is usually self-limited, subsiding in 4 to 10 weeks, although it may at times be subject to recurrences. Occasional cases progress to true rheumatoid arthritis or ankylosing spondylitis.

There are no specific laboratory findings. The sedimentation rate and white blood cell count are usually elevated, while the urine may contain white blood cells, red blood cells, and albumin. Blood cultures give negative results, as do urethral cultures, except for the occasional one positive for PPL organisms; joint cultures and smears give negative results also. The anatomic changes in the synovial tissues are those of nonspecific chronic inflammation, with moderate infiltration of lymphocytes and plasma cells as well as some fibrosis. Roentgenograms are normal initially but may later show bone erosion and osteoporosis, progressing in the persistent cases to narrowing of the joint space indicative of articular destruction.

Treatment is primarily symptomatic; although streptomycin and broad-spectrum antibiotics may appear to be helpful, their use is often disappointing. Hyperthermia, while still used in some clinics, is less popular than formerly. Steroid therapy will bring about prompt reversal of the inflammatory articular signs and in some patients would appear to shorten the duration of the syndrome; others progress to a chronic condition despite all modes of therapy.

Palindromic Rheumatism

Palindromic rheumatism is characterized by frequent attacks of acute short-lived arthritis, recurring at irregular intervals during many years without residual joint damage. The metacarpophalangeal and the proximal interphalangeal joints are the most frequently involved, but any peripheral joints may develop symptoms as may soft tissues at certain sites such as the heels, soles, and finger pads.

Attacks come on rapidly and unpredictably, the involved articulations showing redness, heat, swelling, and tenderness. These persist for from several hours to several days and subside completely, to recur within a matter of days or months. Despite hundreds of such attacks over many years permanent articular damage does not occur.

Early attacks may be confused with gout, but the greater pain and the predilection for the larger joints in that disease usually suggests the diagnosis. Certain cases of rheumatoid arthritis will start with a similar palindromic type of syndrome, progressing after several months or years to a chronic rheumatoid state. The cause of palindromic rheumatism is unknown. Histamine desensitization has been of assistance in a small percentage of patients, suggesting that some cases may be allergic in nature. Symptomatic treatment is usually sufficient; therapy with gold has been employed successfully in patients with protracted cases.

Intermittent Hydrarthrosis

The diagnosis of intermittent hydrarthrosis depends on the finding of recurring painless joint effusions, especially in the knee, without systemic manifestations. The condition is rare; indeed, some question the existence of such an entity. Attacks may occur at regular intervals and last from several hours to several days. Other causes of hydrarthrosis, such as early rheumatoid arthritis, infectious arthritis, and trauma, should be ruled out before the diagnosis is made. Conservative treatment, including use of salicylates, heat, and rest, is usually adequate.

Neurogenic Arthropathy

Neurogenic arthropathy is the term used to designate the enlarged painless joints occurring as a result of nerve injury or disease. They are commonly referred to as "Charcot's joints." The tabetic joint of tertiary syphilis is the best-known example of this condition. The condition, however, is also seen in patients with diabetes, syringomyelia, pernicious anemia, leprosy, spinal cord transection, and peripheral nerve injuries. The underlying pathological lesion is a sensory neural defect which may reside in the spinal cord, posterior ganglion, or peripheral nerves and results in diminution or absence of proprioception, pain, and temperature perception. Injury to the joint occurs because of this loss of sensitivity and the lack of support normally contributed by muscle tone and reflexes. A severe traumatic osteoarthritis ensues. This is characterized by extensive erosion of the articular surfaces, formation of massive epiarticular osteophytes, remolding of the joint contours, and production of loose bodies. Trauma, even of such minor degree as may occur in walking or other normal use, may initiate this degenerative process.

Clinically, the condition starts slowly and painlessly with abnormalities of gait, since the knees and ankles are most commonly involved. The full "Charcot's joint" may then develop rather rapidly, giving a mushy, boggy feeling to the palpating hand. Disability results from mechanical derangement. Roentgenography shows decrease in the joint space, with irregularity and deformity of the articulating bony margins and remolding of the bone, osteophyte production, and bony resorption. Treatment should be of the underlying condition plus mechanical devices designed to assist in weight-bearing. Amputation may be necessary.

Pulmonary Osteoarthropathy

Clubbing of the fingers, together with an ossifying periostitis, usually of the long bones in the region of the wrists and ankles, constitutes the entity of pulmonary osteoarthropathy. It is to be distinguished from benign and heredofamilial clubbing, which is asymptomatic except for the unsightly cosmetic effect. An acute inflammatory reaction may develop in the peripheral joints, particularly in the region of the knees, wrists, and interphalangeal joints, producing a syndrome simulating rheumatoid arthritis. The condition may arise from hepatic and gastrointestinal conditions, as well as from numerous intrathoracic conditions, congenital and acquired, acute or chronic, the most significant of which is bronchogenic carcinoma. Correction of the intrathoracic condition (including removal of certain benign and malignant tumors) brings about prompt remission of the articular symptoms and, at times, disappearance of the clubbing and periosteal elevations.

Psoriatic Arthritis

Although some patients with rheumatoid arthritis suffer from concurrent but apparently unrelated psoriasis, others develop such an intimate relationship between the two diseases as to suggest more than a casual connection. All authorities are not in agreement, but the following three criteria are usually suggested as necessary to the diagnosis of "psoriatic arthritis": 1. Exacerbations and remissions of the two diseases coincide (although the original appearance of either may precede the other by many years). 2. The distal interphalangeal joints are involved. 3. Resorption of bone occurs at the articular margins. In general, the treatment of psoriatic arthritis is similar to that of rheumatoid arthritis. However, because of the possibility of exciting skin lesions, gold therapy must be used with caution. Treatment with steroids, particularly triamcinolone, is of value in relieving the skin condition; severe exacerbations may, however, attend withdrawal.

New Growths

Benign or malignant tumors of joint structures, either primary or metastatic, are rare. Synoviomas have the malignant character of sarcomas of other locations. Diagnosis is established by biopsy but difficulties are encountered on occasion in distinguishing them from certain non-neoplastic lesions. This is particularly true in the case of nodular synovitis (pigmented villonodular synovitis). The latter condition has certain characteristics of a benign neoplasm and of an inflammatory reaction. There is much hemosiderin deposition in the synovial tissues, in addition to giant and xanthoma cell infiltrations. Much of this represents a reaction to intra-articular hemorrhage, but the ultimate origin of the condition is uncertain. Most cases occur in the knee. Related to nodular synovitis is the relatively common tendon sheath tumor (including the giant cell tumor of tendon sheaths). The flexor tendons of the fingers are most often involved. Synovial osteochondromatosis is a rare benign condition in which there is an apparently primary hypertrophic formation of small nodules of cartilage and bone within synovial villi. The nodules are radiopaque and thus produce a characteristic roentgenogram. They may break off into the joint space and cause a secondary osteoarthritis. The knee and elbow are affected most often. Articular complaints in leukemias may result from leukemic infiltration of the synovial or para-articular tissues as well as intra-articular hemorrhage.

Aseptic Necrosis of Bone

Although bone is relatively resistant to ischemic necrosis, because of its multiple sources of arterial supply, infarction may follow total interruption of blood flow such as occasionally occurs in fractures of the neck of the femur. Bone infarcts also occur at times in the absence of demonstrable vascular embarrassment. Such infarcts may be silent clinically unless secondary changes occur in the adjacent joint. The articular cartilage, drawing its nourishment from synovial sources, may retain its viability long after the bone has become necrotic. In time, however, changes in the bone lead to deformity or collapse of the articular surface, and secondary degenerative arthritis results. Such necroses of bone and secondary osteoarthritis are common late sequelae of caisson (decompression) disease.

Juvenile Osteochondritis

Juvenile osteochondritis refers to a group of conditions in which isolated epiphyses undergo aseptic necrosis. The etiology is uncertain. Trauma frequently plays a role, and, in some instances, the lesions arise from mechanical separation of the epiphysis from the rest of the bone. Among the more common sites of involvement are the head of the femur (Legg-Calvé-Perthes disease) and the tubercle of the tibia (Osgood-Schlatter disease).

Osteochondritis Dissecans

Osteochondritis dissecans is a localized form of juxta-articular bone necrosis, followed by dissection and discharge of the dead fragment into the joint space. Most commonly the knee is affected, and young men seem more predisposed than others. The loose body may cause secondary osteoarthritis and should be removed surgically.

Loose Bodies

Loose bodies in the joints, commonly called "joint mice," may produce sufficient irritation to initiate degenerative joint disease. The loose bodies may result from osteochondromatosis, osteochondritis dissecans, loose fragments from intra-articular fractures, fractured menisci, or from the breaking off of osteophytes. When such loose bodies impinge between moving or weight-bearing joints, such as the knee, a temporary painful fixation occurs and hydrarthrosis may follow, requiring surgical removal.

Secondary Arthritis, Arthropathy, or Arthralgia

Many systemic diseases may have accompanying joint or supportive tissue manifestations of varying degree. The more important are discussed briefly here.

Acromegaly.—A severe degenerative joint disease occurs in about one-half of the patients who suffer from a functioning acidophilic tumor of the anterior pituitary. The typical patient, with onset in adult life, demonstrates enlargement of bones and soft tissues of the hands, feet, and face. The features are heavy, the hands large, and the fingers spade-like.

The fingers are most frequently the site of pain, but spine, knees, hips, wrists, and elbows may be involved. Joint motion may be restricted or increased, but stiffness is absent. The affected joints are enlarged. Widening of the joint spaces caused by thickening of the articular cartilage is the most frequent roentgenographic change, but tufting of the terminal phalanges of the fingers and toes and hypertrophic bony changes in the spine and costochondral junctions are also seen.

Ochronosis.—Ochronotic arthritis is the skeletal manifestation of the inherited metabolic disease alkaptonuria. The urine turns black on standing (oxidation) or when an alkali is added. The blue-black ochronotic pigment derived from homogentisic acid is deposited in the cartilage of the ears, nose, and joints as well as in the scleras, endocardium, and meninges. Peripheral articular and spinal disease develops because of the special susceptibility of the pigmented cartilage to osteoarthritic degeneration. The severity of the arthritis varies greatly. Joint symptoms do not begin until the patient reaches adulthood. Loss of mobility and pain on motion in the spine are most common, but shoulder, hip, and knee pain may also be noted.

Roentgenologic studies disclose characteristically thin, calcified intervertebral disks. Degenerative osteoarthritic changes occur in the spine, sacroiliac, and other joints. Treatment is symptomatic.

Hemophilia.—Hemophilia is a congenital disease, usually familial, caused by deficient blood coagulation. In patients over 5 years of age hemarthrosis is the most frequent manifestation of the disease. Repeated bleeding into and around the joint causes permanent damage. Red blood cell lysis and degradation of hemoglobin eventually lead to hemosiderosis of the synovial lining cells, synovial fibrosis, and contracture of the joint capsule, while subchondral and intraosseus bleeding produce cartilaginous erosion and bony cavitation. Damaged epiphyses may close prematurely, and thus normal bone growth may be inhibited. Knees, ankles, elbows, shoulders, and hips are involved in approximately that order, with the small joints of the fingers of the hands much less frequently involved. As hemorrhage into the joint and capsule occurs, the articulation becomes swollen, tender, and warm, with pain on attempted motion. Fever and leukocytosis are present. In time the hemorrhage will be absorbed, but after repeated bleeding episodes deformity and ankylosis may result. Roentgenograms show soft tissue swelling and distention of the joint capsule in the early acute disease, while excavations of subchondral bone and narrowing of the joint space occur later in the disease. Treatment of the underlying bleeding disease with proper blood fractions or whole blood should be instituted as soon as the diagnosis is made. Concurrently, the joint must be rested completely, usually with the patient in bed and elastic bindings applied locally. Joint aspiration may be used when the defective coagulation has been corrected. Treatment with salicylates is helpful in allaying the pain. Physical therapy and ambulation are started when the swelling subsides, and braces may be of additional help.

Menopause.—No form of rheumatic disease is specifically related to the menopause, and the term "menopausal arthritis" is considered a misnomer to be avoided. The onset of osteoarthritic symptoms at this time is coincidental. Reassurance of the patient in this regard may be of significant psychological value in the management of the menopausal woman.

Purpura.—"Henoch-Schonlein" purpura has its most frequent onset with nontraumatic bleeding into the joints or gastrointestinal tract. Spontaneous purpuric or ecchymotic lesions of the skin and viscera may occur with the hemorrhagic arthritis. Remissions and exacerbations over a period of years are common. The cause is unknown; it is not familial. The "Rumpel-Leede" phenomenon is noted, but all other bleeding and coagulation studies give normal results. Treatment is symptomatic.

Serum Sickness.—Delayed allergic reactions to serum or drugs (especially the sulfonamides and penicillin) may occur 7 to 14 days after their administration. Such reactions may involve joints, and this, together with the other systemic symptoms, may mimic rheumatic fever. Joints may be tender and swollen, but the process is self-limited and leaves no residual joint damage. Antihistaminics are of value in treatment.

Sarcoidosis.—This systemic granulomatous disease of unknown etiology may involve the synovium and subchondral bone and may cause mild to moderate arthritis simulating rheumatoid arthritis. It is frequently accompanied by erythema nodosum. Symptomatic therapy and that required for the more severe lung or eye involvements are indicated.

Marfan's Syndrome.—Marfan's syndrome is a heredofamilial disorder of connective tissue, with particular involvement of the ocular, cardiovascular, and skeletal systems. Lenticular dislocation is perhaps the most dramatic, and one of the best-known, manifestations of the disease but is absent in many cases. Myocardial, valvular, and aortic lesions are frequent. Skeletal manifestations include arachnodactylia, increased arm span, excess heel-pubis length in relation to pubis-vertex length, joint effusions, long skull, overly arched palate, excessive joint mobility, patellar hypermobility (and dislocation), pigeon or funnel chest, kyphoscoliosis, winged scapula, and valgus deformities of the knees and ankles. Roentgenograms may also show deformities in the femoral head, pituitary fossae, vertebral arches and bodies, and sacroiliac joints. Bony condensation may be observed in the sacroiliac articulations. Schmorl's nodes, hemivertebra, spina bifida, fused vertebra, and spondylolisthesis may also be noted roentgenographically. Treatment is unsatisfactory and consists primarily of supportive measures, with environmental and occupational regulation to prevent deformities.

Nonarticular Rheumatism

This term applies to a heterogeneous group of conditions producing pain and stiffness in connective tissue structures adjacent to and supporting the joints but not affecting the actual articulation. Relatively few persons go through life without at least one attack of what may popularly be called stiff neck, sore back (lumbago), "neuralgia," or "myalgia." Because such conditions are usually mild and often of short duration the victim usually ascribes such attacks to some overexertion, minor trauma, chilling, or a "cold" and treats himself with home remedies. The physician sees only the relatively small proportion of cases in which the severity or persistence of pain and stiffness forces the sufferer to seek medical assistance. Even so, some rheumatology clinics report as high as 30% of cases classified as nonarticular rheumatism.

Consideration of these disorders as a group is for purposes of convenience only, since causes are diversified and often unknown, while some are poorly defined clinically as well as pathologically.

Calcific Tendinitis of the Shoulder

Calcific deposits in the tendon of the supraspinatus muscle overlying the subacromial bursa may at times become inflamed, giving rise to severe pain in the region of the shoulder, with resultant limitation of motion of that joint. The cause of the calcium deposition is not entirely understood. Small tears in the tendon, with resultant hemorrhage and precipitation of calcium due to pH changes, would appear to be the most likely mechanism. In older persons this is apparently associated with degeneration of the tendon secondary to the constant trauma as it slides beneath the acromial spine. In younger persons acute trauma incident to sudden wrenching or throwing may be the cause. In any event, the deposition of the calcium is not associated with symptoms. Routine roentgenography of the shoulders will show calcium depositions in almost 3% of the population. Once such deposits have occurred they are the potential seat of acute inflammatory reaction, although the precipitating cause of this latter circumstance is obscure. Symptoms come on abruptly, occasionally at night, awakening the patient from sleep. Less commonly, they may start gradually but build up to a peak within 24 to 48 hours. At its height the pain is excruciating and the patient holds the arm tightly to the side, since the least motion aggravates the pain. Acute tenderness is localized sharply to the area of the deposit. The roentgenogram will show a normal shoulder joint with one or more calcific densities of varying size in the supraspinatus tendon. Early, imperfectly formed deposits may not be demonstrable by roentgenologic techniques. In persistent cases cystic areas of degeneration occur in the humeral head.

No treatment is universally effective, and some cases will run a protracted course even with early therapy. Most, however, will respond promptly to injections of procaine or hydrocortisone into and around the affected area. Roentgenologic therapy will bring dramatic relief in some, but in others—particularly after pain has been noted more than six to eight days—it may be ineffectual. Phenylbutazone, in doses of 400 to 800 mg. daily for two to four days, may also provide relief. Physical therapy, in the form of diathermy or ultrasonic soundings, has its greatest usefulness after the acute pain has subsided.

Recurrence of the acute attack months or years later is not uncommon. Multiple deposits or those of unusual size may give rise to chronic symptoms, necessitating surgical removal.

Bicipital Tendinitis

Inflammation of the long head of the biceps brachii as it passes in the intertubercular groove will cause pain in the shoulder. The course is usually less dramatic than that of calcific tendinitis; treatment is similar.

"Adhesive Capsulitis" or "Frozen Shoulder."—"Adhesive capsulitis" or "frozen shoulder" are the terms used to designate the result of muscle atrophy and prolonged immobilization of the shoulder due to calcific tendinitis or bicipital tendinitis. The principle of early motion in acute shoulder pain seems

to be the key to the prevention of the so-called frozen shoulder. Once it has developed it is best treated by physical therapy and intra-articular administration of hydrocortisone.

Shoulder-Hand Syndrome

The shoulder-hand syndrome is a painful disability affecting the nonarticular tissues of the shoulder and hand of the same extremity, similating a variety of rheumatic or arthritic conditions. It sometimes is bilateral. It consists of painful disability of the shoulder preceding, accompanying, or following painful disability of the hand and fingers, in which vasomotor disturbances and diffuse swelling occur. The hand presents features similar to those in causalgia, Sudeck's atrophy, and post-traumatic dystrophy. The symptoms may resolve spontaneously or in response to treatment, or they may progress through various stages to atrophy of the skin, supportive tissues, and muscles of the hands, with contractures—the "dystrophic" features. Patchy to ground-glass osteoporosis, especially at the wrist and head of the humerus, is a frequent diagnostic feature, without other roentgenographically visible change in the articular structures. The syndrome is regarded as an extensive manifestation of reflex neurovascular dystrophy, according to our present limited information.

Although it follows external trauma or internal lesions, the syndrome is also seen without apparent precipitating cause. Seen on medical as well as on surgical, orthopedic, or neurological services, many provocative or associated causes have been reported from the various specialties. Particularly has it been recognized as a complication of internal lesions, such as myocardial infarction, cervical degenerative disease, supraclavicular compression, pericarditis, and cerebrovascular accidents.

The chief differential questions presented by this syndrome arise from its similarities to rheumatoid arthritis, early or late; gout, in the acute onset; and sclerodactylia, in the terminal cases. When the shoulder is affected intrinsic lesions are suggested, but the underlying disease should focus attention on the reflex nature of the complication, confirmed later by hand signs.

Treatment consists of administration of corticosteroids or stellate ganglion block with procaine by serial or continuous administration. Corticosteroids may be prescribed in the daily dosage of 15 to 30 mg. of prednisone or its equivalent. With improvement, the daily amount is reduced by slow decrements, as the clinical response indicates, over a period of weeks or months, until lasting resolution of symptoms is assured. Graduated exercises are instituted as early as is practical within the limits of tolerance. The earlier treatment is begun the more effective it is. Preventive measures are advocated to forestall the development of the shoulder-hand syndrome in known provocative disorders, particularly when atypical pains or vasomotor disturbances are detected in their incipiency. These consist of injections at tender or "trigger" points of procaine or hydrocortisone at the shoulder in the earliest phase, avoidance of pressure or manipulation of the reacting limbs, as well as gentle, gradual exercises as the underlying condition permits.

Dupuytren's Contracture (Contracture of the Palmar Fascia)

Contractures and adhesions of the palmar fascia may be of extremely gradual onset and progression or may appear in a rather short time. Minor trauma may be a contributing factor in susceptible persons. Early cases respond to conservative measures, particularly local heat and corrective exercises, but excision of the thickened palmar fascia may be required in chronic cases.

Tenosynovitis

Tendon sheath inflammation or degeneration may occur alone or in association with definite arthritis. As in subacute or chronic bursitis it may, rarely, be the result of a specific invading organism. The extensor and flexor tendons and their sheaths in the dorsal and volar carpal tunnels at the wrist are most often involved, with the anterior and posterior tibial and peroneal tendons at the ankle next in frequency. Stenosing changes in the tendon sheaths of the abductor pollicis longus and extensor pollicis brevis is called "DeQuervain's disease," but stenosing tendovaginitis may occur in almost any of the tendons of the wrist or fingers.

In most cases conservative management is effective. At times local injection of adrenocortical steroids may be indicated. Incision of the tendon sheath to permit free motion is indicated in persistently painful cases.

Bursitis

Primary inflammatory disease of a bursa is rare. Acute olecranon bursitis may, however, occur in either gout or rheumatoid arthritis, while acute subdeltoid bursitis accompanies calcific tendinitis of the shoulder. Treatment is that of the underlying condition.

Fibrositis

Fibrositis is the term used to identify the common but indefinite condition characterized by stiffness, aching, and pain in nonarticular areas and apparently affecting muscles, facial sheaths, and connective tissue. The most common sites of fibrositis are the paravertebral muscles adjacent to the cervical, thoracic, or lumbar spine, the intercostal muscles, and the trapezii.

Etiology.—The cause is unknown. In some instances acute infections, trauma, unusual physical activity, fatigue, and exposure to dampness and cold appear to be contributory causes. In most patients, however, even these factors cannot be incriminated, and the factor of nervous tension has been increasingly accepted by many students of the condition, thus making a clear-cut differentiation from psychogenic rheumatism difficult.

Pathological Features.—The pathological features have not been clearly defined. Histological studies have been reported variously to show exudation in the connective tissue, small infiltrations of round cells, tender fibrous tissue nodules, and mild degenerative changes in white fibrous tissue and muscles. No consistent changes are agreed on by various students of this disease.

Clinical Features.—Affected persons are usually young or middle-aged adults. A surprising number are under emotional tension. The disorder may begin acutely with a severely painful stiff neck or pain in the lower part of the back requiring bed rest. When so acute the illness usually subsides within 7 to 14 days. Perhaps more commonly the onset is insidious. Aching and stiffness of the neck and shoulders, lower part of the back, or the entire back are common early symptoms. The posterior structures of the shoulder girdle, the interscapular region, and the upper portions of the thighs, especially around the femoral trochanters, are frequent sites of symptoms. Turning, stooping, and twisting motions of the spine, rotation at the shoulders, and lying on the side are difficult to do and aggravate the symptoms. The hands may become stiff, making movement of the fingers difficult and clumsy, with weakening of the grip.

Symptoms and dysfunction have a characteristic diurnal pattern. Generalized stiffness is noted after periods of prolonged rest and is therefore maximal on arising. As the daily activities progress the muscles feel more limber and patients find their optimum period to be the midday. As the day progresses, however, fatigue symptoms develop, forcing early retirement. Dampness, cold, rain, and snow usually worsen the symptoms; warmth, dryness, and the summer season normally relieve them.

Symptoms usually fluctuate and even disappear and recur. The illness may continue for long periods, but seldom is it sufficiently severe to incapacitate the patient; it is more of a "nuisance" disease. Systemic health is good, and fever, loss of weight, and muscle atrophy do not occur. The joints do not show changes. Stiffness limits motion, and the affected parts may be tender. Small, tender nodules are often palpable.

The prognosis is relatively good. The disease frequently subsides or is controlled by treatment, but some cases persist for years. Patients should be assured that they do not have a crippling form of arthritis.

Diagnosis.—The diagnosis is based on the characteristic clinical history, absence of pathological joint changes, normal general health, and negative laboratory findings. Differentiation from early rheumatoid arthritis; mild osteoarthritis, especially of the spine; and psychogenic rheumatism is the chief diagnostic problem. Often the possibility of early rheumatoid arthritis or degenerative joint disease can be excluded only after careful observation of the patient for some time.

Laboratory Findings.—Results of laboratory tests are usually normal. Roentgenograms do not show changes in cartilages or bones.

Treatment.—Treatment of fibrositis is supportive and symptomatic. A middle course concerning restriction of activity and additional daytime rest is advocated. Heat, in the form of hot packs, often relieves pain; massage is usually helpful. Planned exercise done after application of heat may relieve stiffness and aching. Treatment with salicylates is useful for analgesia. Procaine injected into "trigger points" of pain may break the reflex and afford relief for varying lengths of time. Adjustment of the home situation or business difficulties may exert an ameliorating effect on the symptoms. Most observers agree that cortisone or corticotropin therapy is seldom, if ever, justifiable in fibrositis.

Psychogenic Rheumatism

Psychogenic rheumatism is a symptom complex arising from nervous and emotional instability and characterized by pain, soreness, and stiffness in various areas of the musculoskeletal system. It is particularly common in women from the fourth to the seventh decade of life. No pathological lesions can be demonstrated. Indeed, the absence of objective pathology is one of the distinguishing features of the condition.

As noted above, the cause of the condition is to be found in the psychological make-up of the patient, yet it is not limited to any single personality pattern. The appearance of symptoms may unconsciously serve the patient's purpose of gaining atten~~tion or of shielding her~~ from failure in the social or business world.

Although symptoms may come on abruptly during a period of stress, most patients are found to be chronic complainers whose chief delight in life appears to be the recounting of numerous persistent and often bizarre painful episodes. These may be related to any portion—or indeed all—of the musculoskeletal system. Despite a complaint of "agonizing" pain, the patient is usually observed to be in excellent health. Bones, muscles, and joints show no objective evidence of disease, but there is a complaint of widespread tenderness on pressure over the painful areas.

Differentiation between psychogenic rheumatism and fibrositis may be difficult; indeed, some authorities question the existence of primary fibrositis, feeling that the majority of cases so diagnosed are actually cases of psychogenic rheumatism. Nevertheless, certain differences exist. The history of the patient with fibrositis is usually consistent, while the patient with psychogenic rheumatism presents a varying, migratory pattern. This pattern usually has bizarre features which cannot be explained on any anatomic basis. Whereas the patient with fibrositis notes that he feels worse on arising in the morning, better in the middle of the day, and fatigues by evening, the patient with psychogenic rheumatism usually denies any period of spontaneous improvement. Patients with fibrositis are usually adversely affected by cold and damp weather but are relieved by treatment with salicylates. The patient with psychogenic rheumatism usually denies any relationship of the complaint to weather, unless it serves a useful purpose. He also denies benefit from large doses of salicylates, or states that he reacts adversely to them.

Treatment is difficult. Since the patient subconsciously (and apparently, at times, consciously) actually wants or needs the disease, his ego is wounded if he is told that no disease exists. Rather, it seems better to make judicious use of salicylate therapy and physical therapy while exploring with the patient those underlying problems which may be responsible. Formal psychotherapy, while of benefit, is all too frequently rejected by the patient.

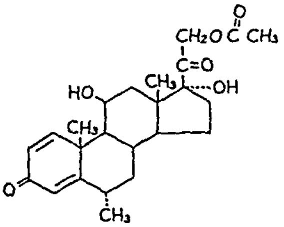
COUNCIL ON DRUGS

NEW AND NONOFFICIAL DRUGS

The following descriptions of drugs are based on available evidence and do not in any case imply endorsement by the Council.

H. D. Kautz, M.D., *Secretary.*

Methylprednisolone Acetate (Depo-Medrol).—6α-Methylprednisolone-21-acetate.—The structural formula of methylprednisolone acetate may be represented as follows:



Actions and Uses.—Methylprednisolone acetate shares the actions and uses of the parent compound, methylprednisolone. (See the monograph on methylprednisolone in New and Nonofficial Drugs.) Aqueous suspensions of the drug are suitable for intrasynovial and soft tissue injection and thus may be used for the local treatment of rheumatoid arthritis, osteoarthritis, tendinitis, bursitis, and other conditions that are responsive to the anti-inflammatory action of gluco-corticoids. When used in this manner, the effect of methylprednisolone acetate is comparable in intensity and duration of action to that of other relatively insoluble steroid compounds, but slower in onset and of longer duration than that of the highly soluble salts. In addition, methylprednisolone acetate may be administered by intracutaneous or intralesional injection for the treatment of susceptible dermatological conditions. The drug is also suitable for systemic therapy and, when administered intramuscularly, may be expected to produce the effects of orally administered methylprednisolone. It has been incorporated in retention enemas, which have been tried experimentally in the management of ulcerative colitis; although not all patients respond favorably, some experience marked improvement.

Methylprednisolone acetate apparently produces little or no pain or irritation after injection into the joint spaces or soft tissues. Systemic effects after local use have not been reported. Rapid settling of the drug may occur, however, if its suspensions are mixed with solutions of local anesthetics; such mixtures are rarely required. Intra-articular or other injection for local effect is contraindicated in the presence of acute infection. Precautions, contraindications, and undesirable effects described for the oral use of methylprednisolone are applicable also to the intramuscular use of methylprednisolone acetate.

Dosage.—Methylprednisolone acetate is administrated by intramuscular, intrasynovial, or soft tissue injection. For intra-articular injection, the dose required varies with the size of the joint and the degree of inflammation. For large joints, such as the knee, ankle, or shoulder, 20 to 80 mg. may be required; for the elbows or wrist, 10 to 40 mg., and for smaller joints, 4 to 10 mg. In the management of bursitis, tendinitis, or epicondylitis, 4 to 30 mg. is administered in a single injection, which may be repeated as required. For local injections in dermatological conditions, doses of 20 to 60 mg., depending on the size of the lesion, may be employed.

For systemic effects, such as in rheumatoid arthritis, methylprednisolone acetate is administered intramuscularly in a single dose of 40 to 120 mg.

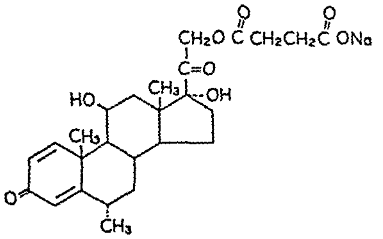
per week. If daily administration is preferred, the dose is approximately the same as the oral dose of methylprednisolone.

Preparations.—suspension (injection) 40 mg. in 1 cc., 200 mg. in 5 cc.

Year of introduction: 1959.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of methylprednisolone acetate.

Methylprednisolone Sodium Succinate (Solu-Medrol).—Sodium 6α-methylprednisolone-21-succinate.—The structural formula of methylprednisolone sodium succinate may be represented as follows:



Actions and Uses.—Methylprednisolone sodium succinate has the same metabolic and anti-inflammatory actions as methylprednisolone. Because it is highly soluble and can be administered in small volumes of diluent, it is useful for parenteral injection in situations in which a prompt and intense hormonal effect is indicated. Equimolar amounts of parenterally administered methylprednisolone sodium succinate and orally administered methylprednisolone have the same biological activity.

Parenterally administered methylprednisolone sodium succinate is intended primarily for short-term emergency therapy. Under these circumstances, typical steroidal side-effects are not likely to become a problem. The drug is subject to the same contraindications as other systemically administered agents of this class. (See the general statement on gluco-corticoids in New and Nonofficial Drugs.)

In a small series of patients, methylprednisolone sodium succinate has been administered rectally in the form of retention enemas for the management of less severe cases of ulcerative colitis. Results have been promising. Thus, in the majority of cases, clinical improvement has been noted within three days after institution of therapy; favorable proctoscopic changes have been observed within one week. These results suggest that, by the rectal route, improvement may be anticipated more promptly than when orally given steroids are employed. However, considerably more clinical experience with this relatively untried procedure is necessary before it can be routinely advised.

Dosage.—For parenteral therapy, methylprednisolone sodium succinate is administered by intravenous or intramuscular injection or by intravenous infusion. The intravenous route is preferred for initial emergency therapy. The usual dose for intravenous or intramuscular injection is 40 mg.; frequency of administration is governed by clinical response. For intravenous infusion, a solution containing 40 mg. in 1 cc. is diluted with appropriate volumes of 5% dextrose in water, isotonic saline solution, or 5% dextrose in isotonic saline solution, and administered by slow drip.

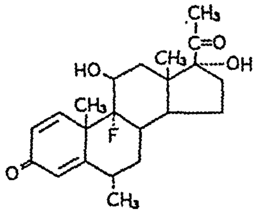
For rectal use in patients with ulcerative colitis, solutions containing 40 to 120 mg. are added to varying amounts of water and administered as retention enemas three to seven times weekly for periods of two or more weeks.

Preparations.—powder (injection) 40 mg. with 1 cc. of sterile diluent.

Year of introduction: 1959.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of methylprednisolone sodium succinate.

Fluorometholone (Oxylone).—9α-Fluoro-11β,17α-dihydroxy-6α-methyl-1,4-pregnadiene-3,20-dione.—The structural formula of fluorometholone may be represented as follows:



Actions and Uses.—Fluorometholone is a highly potent gluco-corticoid which is used exclusively for its anti-inflammatory effects on the skin. The drug shows a marked specificity of anti-inflammatory action with topical application. Thus, it is approximately 40 times as potent, on a weight basis, as hydrocortisone when applied to the skin but is equipotent with hydrocortisone when administered orally. Because of this greater specificity of local over oral activity and the consequent low doses required for local effects, undesirable systemic hormonal effects due to possible absorption of the steroid from the skin are highly unlikely.

Fluorometholone is effective by topical application for the treatment of acute or chronic dermatoses that have an allergic or inflammatory basis and are associated with pruritus. These include contact dermatitis, atopic dermatitis (including allergic eczema, neurodermatitis, and eczematoid dermatitis), seborrheic dermatitis, pruritus with lichenification, and nonspecific anogenital pruritus. Although no clear-cut superiority has been demonstrated, the results of therapy with fluorometholone have been comparable to those obtained with other steroids known to be satisfactory for these skin disorders. In view of its specificity of anti-inflammatory action when used topically, fluorometholone appears to be well suited for the management of allergic dermatoses.

As with other topically applied steroids, fluorometholone should not be used on infected areas of skin unless appropriate anti-infective therapy is instituted simultaneously. The drug is contraindicated in the presence of tuberculosis of the skin and should not be applied to the areas adjacent to the eye in patients with ocular herpes simplex. There is no evidence of local irritation or sensitivity after the topical use of fluorometholone.

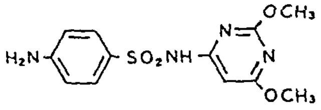
Dosage.—Fluorometholone is applied topically. A preparation containing 0.025% fluorometholone is rubbed into the involved areas of skin one to three times daily.

Preparations.—cream (topical) 0.025%.

Year of introduction: 1959.

The Upjohn Company cooperated by furnishing scientific data to aid in the evaluation of fluorometholone.

Sulfadimethoxine (Madribon, Madriqid).—N'-(2,6-Dimethoxy-4-pyrimidyl) sulfanilamide.—2,4-Dimethoxy-6-sulfanilamido-1,3-diazine.—The structural formula of sulfadimethoxine may be represented as follows:



Actions and Uses.—Sulfadimethoxine, like sulfamethoxypyridazine, is characterized by slower renal excretion and more prolonged blood levels than most other sulfonamides. However, it resembles other members of this group in its antibacterial spectrum, side-effects, and indications for use. (See the general statement of sulfonamide compounds in New and Nonofficial Drugs.)

Oral administration of sulfadimethoxine produces peak blood levels within four to eight hours, depending on the size of the dose. After administration of 2 Gm. initially, followed by 1 Gm. daily, peak levels are maintained on a plateau. Larger doses, however, may produce cumulation and a gradual rise in the blood sulfonamide concentration.

Approximately 85% of the sulfadimethoxine in the blood is in the active form; 10% is present as the acetyl derivative, and the remainder is a glucuronide. The exact structure of this glucuronide, as well as the site of its metabolic formation, is unknown. Antibacterial activity of the metabolite cannot be demonstrated.

Sulfadimethoxine is excreted in the urine. Approximately 5% appears in the unchanged form, 15% is acetylated, and 80% appears as a glucuronide. Roughly one-half of a single oral dose of 2 Gm. can be recovered from the urine within 48 hours after administration. On a constant drug intake of 1 Gm., about 80% of the drug is excreted daily. Sulfadimethoxine and its acetyl derivative have exceedingly low solubilities in acid solutions, but the solubility of the major excretion product, the glucuronide, is quite high, exceeding 2,000 mg. per 100 cc. at a pH of 6.0.

Sulfadimethoxine has been employed successfully for the treatment of certain bacterial infections of the soft tissues and respiratory tract. Results in urinary tract infections have also been satisfactory, despite the fact that the sulfonamide is present in the urine largely as the inactive glucuronide.

Side-effects observed with the use of sulfadimethoxine, such as nausea, vomiting, and skin eruption, are essentially the same as those previously reported for other sulfonamides. No reports of crystalluria, hepatic damage, or blood dyscrasias have yet appeared. As with other sulfonamides, administration of sufficient fluid to maintain a daily urine output of 1,000 cc. or more seems advisable; when the drug is given over a prolonged period, hematological studies should be performed at regular intervals.

Dosage.—Sulfadimethoxine is administered orally. Because of its relatively slow excretion, a single daily dose is sufficient to maintain adequate blood levels. For mild infections in adults and children weighing 80 lb. (36.3 kg.) or more, an initial dose of 1 Gm., followed by 500 mg. daily, may be tried. For more severe infections, doses up to twice as great may be necessary. In children weighing less than 80 lb., doses of 12.5 to 25 mg. per pound of body weight, depending on the severity of the infection, are suggested for initiating therapy. One-half of the original dose is then given every 24 hours.

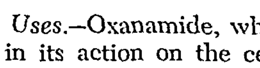
The appropriate daily doses of sulfadimethoxine may also be given in divided amounts; one-fourth of the daily dosage previously stated is administered every six hours.

Preparations.—capsules 125 mg.; suspension (oral) 50 mg. per cc.; suspension (oral drops) 250 mg. per cc.; tablets 500 mg.

Year of introduction: 1958.

Hoffmann-LaRoche Inc. cooperated by furnishing scientific data to aid in the evaluation of sulfadimethoxine.

Oxanamide (Quiactin).—2-Ethyl-3-propylglycidamide.—The structural formula of oxanamide may be represented as follows:



Actions and Uses.—Oxanamide, which resembles meprobamate in its action on the central nervous system, produces a calming effect that is often useful in the management of psychoneuroses, the major psychoses, and aberrations of behavior associated with cerebral arteriosclerosis and other disorders. The drug is most effective when the predominant symptom is anxiety or tension, regardless of the underlying cause or clinical diagnosis. Patients who respond may display an improvement in general behavior, lessening of anxiety and depression, and an increased interest in the environment. Psychosomatic symptoms, such as tension headache, may also respond to oxanamide. Its use in psychotic patients may permit a reduction in the frequency of electroshock therapy and may facilitate social readjustment by decreasing quarrelsomeness and irritability; a few patients show sufficient improvement to allow paroling from institutions. Oxanamide has not been employed for quieting acutely disturbed patients and, because of the relative mildness of its central depressant action, is probably not suitable for this purpose. A definitive assessment of the relative efficacy of oxanamide, in comparison with other similar drugs, must await further clinical testing; that it is more efficacious than older drugs has not been established.

Pharmacology.—Oxanamide is well absorbed after oral administration. In animals, only 10% of a single dose is excreted in the urine; the fate of the remainder is unknown. The disposition of the drug in man has not been determined; no evidence of cumulation has followed repeated administration of usual doses to human patients.

Laboratory studies indicate that oxanamide is primarily a central nervous system depressant. It appears to be an internuncial neuronal blocking agent, to inhibit polysynaptic reflexes, and, by means of these central actions, to produce a degree of skeletal muscle relaxation. Large doses have also been reported to exert a hypnotic effect similar to that of short-acting barbiturates. The precise pattern of activity of oxanamide on the central nervous system, including possible interaction with transmitter substances, has not been determined.

Side-effects.—Oxanamide is remarkably free from serious toxicity. No adverse effects on renal, hepatic, or hematopoietic function have been reported. Drowsiness may occur but is infrequent and usually appears only after large doses. In normal individuals, doses of 800 mg. do not alter reaction time or performance in complex tasks such as those involved in driving. Oxanamide has not, as yet, been reported to cause habituation or addiction. Withdrawal symptoms have not been seen after discontinuance of therapy. However, present experience is much too limited to justify a definite assumption that the drug is devoid of addicting potentiality.

Dosage.—Oxanamide is administered orally. The usual dose is 400 mg. given four times daily, but this should be adjusted to meet the needs of the individual patient. For sedative effect, 800 mg. may be given at bedtime.

Preparations.—tablets 400 mg.

Year of introduction: 1958.

The Wm. S. Merrell Company cooperated by furnishing scientific data to aid in the evaluation of oxanamide.

COMMITTEE ON REHABILITATION

The following report is the third in a series of articles which have been authorized for publication by the Committee. The first two appeared in the Oct. 24 and Nov. 7 issues of The Journal, *pages 1107 and 1359. This series deals with various aspects of rehabilitation which are of interest to physicians.*

Ralph E. De Forest, M.D., *Secretary.*

SOCIAL WORK IN REHABILITATION

Jayne Shover, M.A., and Oscar Kurren, M.S.W., Chicago

During much of the early practice of social work, the profession was almost exclusively concerned with problems arising from poverty. For many, social work is still erroneously synonymous with the dispensing of public assistance. We have developed methods of maintaining relative economic stability and have available such a wide variety of public and private resources, however, that poverty is no longer the major problem today that it was at the turn of the century. Mass poverty has been displaced by other major problems that have developed out of increased industrialization and population changes.

Management of the chronically ill patient now constitutes one of these major problems. Estimates of the U. S. Public Health Service currently indicate that there is a handicapped population of 9 million persons in need of, or who can benefit from rehabilitation services, with 250,000 persons being added each year. Statistics often lose their impact when presented in this fashion. To the physician who daily must make decisions and develop treatment programs for the patients who come to his office with major disability problems, such as cerebral palsy, cerebral vascular accidents, spinal cord disease, multiple sclerosis, arthritis, and heart disease, chronic illness is very real. The combined medical-social problems for patients with these illnesses assume serious proportions.

Associate Director, National Society for Crippled Children and Adults, Inc. (Miss Shover) and Consultant on Rehabilitation Facilities, National Society for Crippled Children and Adults, Inc. (Mr. Kurren).

Rehabilitation as a concept of total patient care, comprising a definite body of knowledge and procedure, has come to the forefront in meeting the many-faceted problems of chronic disease and disability. Rehabilitation cannot be identified solely as *physical therapy, occupational therapy, or a* particular specialized branch of medicine. It is all of these and more. Various aspects of physical restoration constitute but one facet in the total rehabilitation process. As Dr. Howard Rusk so aptly states:

> Rehabilitation is not just splints, crutch walking, and the like. It has to meet the total needs of the individual; those needs are physical, emotional, social, and vocational, and at any time you miss a cog in the link then your morbidity goes up, and also your mortality; not the mortality of death but the mortality of something that is sometimes more than death, mortality of living a life of indignity, of dependency and depression.

Rehabilitation programming includes physical restoration services, comprising medical evaluation and treatment and physical and occupational therapy; speech rehabilitation; social services, which may include parent counseling services; psychological services; special education; vocational services, including workshops; recreation services; and health education. In the large metropolitan areas these services have been developed within the framework of the comprehensive rehabilitation center, where each professional discipline concerned with rehabilitation contributes toward provision of a coordinated program, geared to meeting total needs of the patient.

Experience has demonstrated that the rehabilitation of an individual is ultimately dependent upon the patient himself. Benefits of many a carefully planned treatment program have been nullified because of the patient's inability to follow recommended procedure. Many a paraplegic, who has been instructed to shift his sitting position from time to time so as to relieve pressure and prevent stoppage of circulation, has neglected to follow this important recommendation and has subsequently returned to the hospital for plastic surgery because of the development of decubitis ulcers. The amputee, who has been advised not to place his stump on a pillow so as to avoid contractures, may disregard this and be readmitted with presence of extensive flexion contracture. Carefully planned dietary regimens are often violated by the diabetic, though he possesses the knowledge that doing so will result in aggravation of already existing physical problems. Many cardiac patients return to work situations involving excessive stress, in spite of warnings by the attending physician.

What causes this resistance to rehabilitation? It can be understood only when there is an analysis of what the disability means to the patient. Rehabilitation must start then at the point of diagnosis. Much of the present chronicity of disease, extensive deformity, and resultant social, emotional, and vocational dislocation could have been avoided if, at the time of diagnosis, there were recognition of the need to initiate comprehensive rehabilitation programming or, more precisely, total patient care.

Diagnosis for rehabilitation encompasses determination not only of the nature and cause of the disability in terms of pathology present but also of an appraisal of social, psychological, and environmental factors. It is at this point that the social worker can make specific contributions to planning a program of total patient care. These include (1) understanding of the patient's situation prior to disability, his vocational and economic circumstances, and his goals; (2) evaluation of the patient in relation to his family constellation, with emphasis on the patient's and family's knowledge and acceptance of disability and of rehabilitation planning; and (3) appraisal of the personal and cultural forces that shape and determine the individual's reaction to disability. The social worker, working with the physician and other members of the rehabilitation team, gears his efforts to achieving understanding, insight, and acceptance of the disability by the patient and his family and obtaining their cooperation in the treatment program.

A primary responsibility of the social worker is to assist the patient in effective utilization of the services available to him. This is a shared responsibility with other members of the rehabilitation team, but the major responsibility for helping the patient bridge the gap between hospital experience and the rehabilitation center, or from a long-standing homebound status to the activity of the rehabilitation program, rests with the social worker.

Social work skills are essential in helping parents make the adjustments required in coping with the problems engendered by chronic long-term illness in children, for it has been found that success in these adjustments depends much less on the severity of the physical handicap than it does on satisfactory quality in relationships between parent and children and rewarding social experiences and achievement in the community.

Physicians are finding it increasingly difficult to maintain the much valued and traditional physician-family-centered relationship in the face of pressures of modern medical practice. The impact of scientific advances has brought many changes in structure and organization of medical care and has led to increased fractionization of professional services. We live in an age of specialization and the use of specialized institutions. It is the rule, rather than the exception, for the physician to treat the patient outside the framework of the patient's family and home in the impersonal environment of the hospital or physician's office. The wide chasm that now exists, separating the patient's way of life at home from his hospital experience, poses problems in patient care and treatment. Dr. John Paul has described present-day limitations in the teaching of medical students:

> These sick people are isolated specimens. They are segregated from their environment, removed from the circumstances under which they became ill, separated from their families, stripped even of their clothes; all of which is done to create a proper atmosphere for diagnostic study and careful management on the physician's part, free from "outside distractions." It may be trite to point out that these outside distractions are the very things which the modern doctor, or a student interested in preventive medicine, needs to study also. For if one is to handle patients adequately it is necessary to bring clinical judgment to bear, not only on the patient, but also on the circumstances under which his illness arose.

Much of the activity of the social worker in rehabilitation is in reinforcing the effectiveness of the treatment program. This is clearly demonstrated in the following case example.

Jim Young, a 30-year-old paraplegic, had been making steady progress at the rehabilitation center until the third month of his stay, when he began to withdraw from therapy activities, a time in his program when a trial visit to his home was under consideration. In interviews with the social worker, Mr. Young expressed fear and anxiety over returning home. For the first time since his accident he was faced with the reality of returning to his wife, children, and community. He no longer regarded himself as "a whole man" and found it difficult to face being thrust into a changed role in his home where he had always been a most adequate husband and father.

Case work services with Mr. Young were directed toward helping him better understand and accept his reactions to his disability and to mobilize his potential for achieving full resumption of life activities. The total treatment process was considerably facilitated when the social worker secured the direct participation of Mr. Young's family in the rehabilitation program, thus easing transition between the rehabilitation center and the home.

One of social work's most important functions is in community planning for rehabilitation. Social work has been called "a profession sitting on the fence" where this responsibility is concerned.

All professions engaged in rehabilitation planning, including social work, must accept the challenge to help make available to the community an integrated rehabilitation program. Development of adequate communication among the various professions is essential as a first step towards achieving this goal. Personnel engaged in rehabilitation must have the vision, ability, and maturity to work within a multidisciplinary program. There is a give and take in the rehabilitation process which makes it impossible for the professional worker to limit himself to his own narrow sphere of activity.

The intrinsic character of social work places emphasis on knowledge, utilization, and development of community resources. No one program in rehabilitation can embody all the services required by the severely disabled; the complex nature of rehabilitation programming and the fast-changing community scene call for more than a sporadic, part-time approach. Thus, expertness is essential in making appropriate use of the full spectrum of medical, psychological, social, recreational, educational, and vocational services needed. The social worker on the rehabilitation team has the specific charge and competence to assume responsibility in this area.

Summary

In summary, the role of the social worker in rehabilitation involves bringing to bear his special competencies and skills toward (1) developing a better understanding of the person, his family, and environmental factors that can spell the success or failure for achieving rehabilitation goals; (2) interpreting this new knowledge clearly and effectively to other members of the rehabilitation team so that there exists unity of purpose and action; and (3) evaluating the community and its total resources and selecting the appropriate service so as to insure and protect the gains achieved by the patient in his rehabilitation program.

The social worker can help achieve the fine balance required that will lead to a satisfactory productive life experience for the disabled person.

A HAZARD IN THE HOME MEDICINE CABINET.—The symptoms of atropine poisoning have been described as follows: "Hot as a hare, blind as a bat, dry as a bone, red as a beet, and mad as a hen." . . . A recent experience with atropine poisoning was encountered after a patient frequently flushed his nasal passages with an atropine sulfate solution previously prescribed for his dog. His symptoms were characteristic of this condition, but the manner in which it was incurred was not known until several hours after his acute problem required treatment. It is fortunate that this potent drug is infrequently found in the home medicine cabinet, but every clinician needs to be aware that accidental poisoning from atropine may be encountered in his practice. The public should continually be educated to discard medications that no longer are in active use.—G. M. Hoffman, M.D., and J. R. Gay, M.D., Accidental Atropine Poisoning, *The Pennsylvania Medical Journal*, September, 1959.

MEDICINE AT WORK

- *Sports Medicine Meeting*
- *Trouble Shooting Clinic*
- *Primer for Homemakers*
- *Ahead in Legislation*
- *Science and the A. M. A.*
- ✓ *Families for the Aged*

Image and Imagery

The changing image of the physician and his vocabulary has evoked comment in three state medical journals recently:

From *Virginia Medical Monthly*—"The faster medicine advances scientifically, the faster the feeling of friendship between the physician and his patients deteriorates from the beloved image of the country doctor. Out of this erosion there is developing a public attitude which, under political and economic pressures, can be dangerous for our profession. . . . We must do what we can—each in his own way—to improve the public's attitude toward the medical profession."

From *Missouri Medicine*—"There is an occupational hazard in the practice of medicine that, if not guarded against, can do the individual doctor, the profession, and society a great deal of harm. It is the temptation for doctors to think of themselves as individuals set apart from the rank and file of humanity, set apart by knowledge, skill, and power. . . . Somehow we get to feel that we are entitled to an acquiescent 'Yes, Doctor,' from the whole human race on any matter whatsoever."

From the *Journal of the Medical Society of New Jersey*—"In addition to housemaid's knee, trolley eye, [and] chimney-sweep's disease, we have—or used to have—miner's nystagmus, hatter's paralysis, coffin joint, diver's palsy, bricklayer's itch, writer's cramp, painter's colic, soldier's heart, cobblestone tongue, mossy foot, and rake teeth. . . . [But now] our vocabulary, like the operating room, is becoming a model of sterility."

Children try talking out their problems in Trouble Shooting Clinic in Queens, N. Y., to Dr. Lester R. Tuchman, *left*, who heads hospital board, and Dr. Alonzo Beavers of clinic staff.

Walk in and Talk

This "Trouble Shooting Clinic" Is Strengthening a Community

Milton Golin

As in many another hospital, your heels click along the wide corridor during your stroll toward the small signpost at one end of the main floor. Below the words, "Trouble Shooting Clinic," is an arrow. You follow the direction and in a few steps you are there—together with:

—A shoe clerk in trouble with his mother-in-law.

—A stenographer troubled with her jealous boyfriend.

—A busy housewife facing trouble with "feuding neighbors."

—An elderly widower troubled with his "crazy" son.

—A high school student engulfed in the troubles of her broken home.

—A truck driver troubled by the death of a loved one.

Troubles all around (see Medicine at Work, The Journal, *Nov. 8, 1958).*

This is the City Hospital at Elmhurst, in Queens, N. Y., where, since September, 1958, more than 750 men, women, and children have stepped out of the busy traffic of Broadway in a search for peace from some particularly anxious incident in their lives. It is the only "walk-in" clinic of its kind in the world. It is an emotional first-aid station. It is a promising experiment in preventive psychiatry. Even more important, perhaps, it is a focus of community strength in a metropolis where, according to some conceptions, community concern for the individual does not exist.

"Significant elements of the community are, in fact, keys to the clinic operation," says Dr. Lester R. Tuchman, a Manhattan internist who serves as president of the hospital board. "Not only are we learning more about the resources available in Queens for our work but the community is getting to know us a little better. Many of those who walk in have heard about us from their minister or a local attorney or a family or religious service organization or even from a cop on the neighborhood beat."

Most, however, are self-referred, which indicates, according to

Dr. Tuchman, that their personalities are well enough organized to reach out for help. Primarily to accommodate them after work, regular hours are 6 to 9 p. m. on Tuesday and Thursday evenings, although sympathetic treatment outside the scope of the clinic's multidisciplinary approach is available at all other hours in the hospital emergency room. No appointment is required, and nobody is turned away. Usually, in a single clinic interview the trouble can be handled; seldom is the maximum of three hourly visits necessary. In the few cases in which prolonged treatment is indicated, efforts are made to get the patient to his family physician, to a psychiatrist or private psychiatric clinic, to his minister, or perhaps to a social or legal agency. Occasionally, hospitalization is recommended.

"The troubles of these people are not trivial," says soft-spoken Dr. Alonzo J. Beavers in his trace-of-Texas twang. "Everyone arrives with a sense of urgency, a sense of impending personal disaster. The clinic acts as a safety valve where they can talk out their troubles and prevent an explosion."

Dr. Beavers is the assistant director of psychiatry, serving under Dr. Leopold Bellak, the prime mover of the Trouble Shooting Clinic. Both are principally engaged in private practice. Also on the clinic staff are Mrs. Josephine Scott, M.S.W., the chief social worker, and Paul Park, Ph.D., the chief psychologist. Their roles in screening and interviewing are woven into the total medical approach.

One-Hour Solution

One success of the team effort was chalked up recently when a young man, broke and out of work, walked into the clinic in a frazzle of worry over his inability to obtain a cabdriver's license so he could support his wife and three children. The city had refused him a license on the basis of an army medical discharge for psychoneurosis. Within one hour, these things happened: The clinical psychologist determined that the man had the necessary intelligence, the social worker learned from a nearby police station what would be needed to satisfy authorities for the issue of a license, the psychiatrist decided that the psychoneurosis was not severe enough to interfere with the job, and—as a result of all this—the hospital handed the man an official statement that he was capable of handling the responsibility of taxi-driving. He got the license.

Woman who walked in for help is interviewed in Trouble Shooting Clinic by Dr. Beavers. In right foreground is Dr. Leopold Bellak, director of psychiatry and moving force behind clinic. Hospital board sought him out to establish it.

Emotional First Aid at Home

Another "emotional first aid" facility is operating in suburban Boston. At Mattapan, Mass., the Psychiatric Home Treatment Service—like the Trouble Shooting Clinic in New York (*see story*) —uses the psychiatrist-psychologist-social worker team approach to give emergency treatment. Unlike the New York clinic, PHTS functions on a mobile basis, responding to emergency calls from physicians, social agencies, private families, and clergymen. The Massachusetts service, too, is a vehicle for mental health education at both the family and community levels. It was begun in January, 1958, under the joint auspices of Boston University School of Medicine and the National Institutes of Health. Dr. Tobias Friedman, head of the mobile psychiatric unit, has reported, "Emergency treatment for emotionally ill persons who will not or cannot get hospital care is a crucial and universally neglected problem."

Such duties of the four clinic members are combined with broader staff responsibilities in the 1,000-bed city hospital. Not overlooked in these broader responsibilities is the opportunity to extend both general and medical education in mental health. This month, for example, the hospital's five chaplains (see Medicine at Work, The Journal, April 13, 1957) are scheduling a seminar with other clergymen of the community to discuss the work of the Trouble Shooting Clinic. And, at frequent intervals, 10 hospital residents sit in on selected cases. This equips them, at ensuing sessions with the clinic staff, to help analyze the diagnostic and therapeutic techniques employed for individual patients.

Community Asset

"In such a learning-teaching process," says Dr. Beavers, "we see unsophisticated patients who might never walk in if the clinic had a title with 'psychiatric' or 'mental' in it. Too frequently, still, they equate psychiatry with something for 'crazy' people. But they do come for help when they trust the clinic as a place where they can be helped with those everyday problems which might erupt into major troubles, a place where they may get first aid for upsets and bruised feelings.

"This clinic in this hospital in this community does not represent a special kind of situation for success. The concept of trouble-shooting, in the general pattern which we have been following, is eminently suited to any community hospital serving its environs. It is a distinct asset to the community, not only because the majority of the troubles—85% here at Elmhurst—are handled effectively, but also because of the definite preventive medicine aspects. That is our long-term goal—prevention. The true value of this clinic is not in the visible accomplishments—like the cabbie who got the license—but in what cannot always be seen—a suicide averted here, a homicide prevented there, an entire family held together by the resolution of a single problem. Those are situations which cannot be measured."

Darwin's Theory Is Getting A Grand Centennial Salute

One of the world's most impressive scientific meetings will open next week after nearly four years of planning. For five days, beginning Nov. 24, 50 leading authorities in fields ranging from astronomy to zoology will discuss the impact of Charles Darwin's ideas on evolution. His theory was published Nov. 24, 1859.

The Darwin Centennial Celebration, centering at the University of Chicago, also will project his theory into its likely development in centuries ahead, as scientists examine everything from the tiniest particle of living matter to the destinies of outer space. More than 1,000 persons from throughout the United States and abroad will be attending the celebration to hear unrehearsed panel discussions on The Origin of Life, The Evolution of Life, Man As a Biological Organism, The Origin and Nature of Mind, and Social and Cultural Evolution. Ten nations, including the Soviet Union, are sending scholars. Specific medically oriented topics to be discussed in relation to evolution include viruses, diseases of the mind, cancer, nervous function, genetics, anatomy, and physiology.

"The celebration will be a milestone in the history of evolution," says Sol Tax, chairman of the centennial committee. "It will be the most comprehensive and intensive examination of the impact of Darwin's ideas on all aspects of man and his universe ever held at one time and place."

To Help Chart a Course for A. M. A. Scientific Activity

A telescopic image of future A. M. A. scientific activity soon might be looming into view on a lens focused by some of America's leading physicians and scholars. For two and a half days in Hershey, Pa., members of the Board of Trustees joined with educators in medicine and allied sciences, practicing physicians, administrators, A. M. A. staff personnel, and research leaders to examine closely the Association's present role in medical science.

This week the Board of Trustees, whose Committee on Scientific Activities sponsored the conference, was scheduled to discuss the happenings at Hershey, where Dr. R. B. Robins had said, "We on the Board will be considering the fine suggestions you have made so that we may in turn offer to the House of Delegates recommendations on how to improve the scientific activities of the A. M. A." As if to underscore that point of implementation, John S. Millis, Ph.D., president of Western Reserve University, said:

"The A. M. A. is a voluntary Association, and that which is done is not done by the decision of a dictator or of a single group of men and women but rather by the voluntary decision of a group of free men deciding that which is wise and prudent and moral. . . . The A. M. A. is the greatest force within the fabric of medicine which is concerned with supplying a unifying force to be a counteraction to those forces which divide medicine itself."

Dr. Millis was speaking as chairman of the 20-member ad hoc committee whose members were selected (see list in Medicine at Work, THE JOURNAL, Sept. 12, 1959) for their scientific eminence and also because their detachment from A. M. A. organizational matters equipped them with an objective overview. The meetings Sept. 14 through 16 progressed in an atmosphere of constructive criticism interlaced with bold suggestions (see box) which bristled with controversy. It was an atmosphere in which scores of provocative questions, such as the following, sometimes contributed more to discussions than did answers:

—Should the A. M. A. take direct action calculated to arouse active interest in creating new medical schools?

—Should a reevaluation of all A. M. A. committees be made to determine whether there are duplications of activities?

—Does the A. M. A. as a whole attempt to do too much or too little, scientifically?

—Should A. M. A. membership include scientists other than physicians, who are working on medical problems?

—Is a "Doctor Relations" (doctor-to-doctor) program in the area of medical sciences more impor-

Bold Words at Hershey—Will They ....

On both sides of a two-way mirror, A. M. A. scientific activity was given a critical once-over at Hershey, Pa., by men and women inside as well as outside of the Association. It was inevitable that their inspection-introspection should produce frank and provocative statements. Here are a selected few:

On education and medical schools—

Too many medical schools adopt grade-school and high-school methods. We should regard medical students as true graduate students—recognizing that it is just as important to teach what is not known about a subject as what is known. . . .

One might well consider abolishing departments of pathology and anatomy, and integrating the study of normal structure with normal function. This may seem heretical, yet the divorce of structure from function is obviously illogical. . . .

There is a contradiction in the fact that the A. M. A., in one breath, says, "We will not recognize your medical school until it has these certain courses"—and then, in the next breath, says, "Sorry, you cannot accept federal funds to help establish these courses, because only construction funds are acceptable from the government. . . ."

If medicine is concerned only about medical education, as we normally think about it in the medical school or hospital, we are blinded; for the health of medical education is no greater than the health of the total educational enterprise. . . .

There are situations in which the competition, jealousies, and rivalries among physicians are such as to virtually insure that a physician's work will not be scrutinized by his colleagues. Group practice would appear to be one convenient organizational structure through which a physician could be better exposed to a thorough medical audit by his colleagues. It also seems to be an ideal mechanism for the participation of its members in formal educational opportunities. . . .

The A. M. A. would gain much public approbation if it would estimate the number of new medical schools needed, specify the geographical areas where they are needed, and not attach any strings to funds which would build these schools. . . .

Yet this is many-faceted. We cannot simply recommend more medical schools. We must tie that in with the need for more medical faculty. . . .

We might consider creating a type of medical man who does not now exist in America—a man able to perform tasks beyond those generally assigned to a registered nurse, but who is qualified to perform some of the functions of a physician only under the physician's supervision. . . .

On research—

There is really only one issue on which the future of medical science depends. That is to insure that we continue to maintain and expand the opportunities in medical research for those who, by their natural gifts of mind, are able and willing to carry out the exacting tasks that lead to advancement of knowledge. How much money is needed, who should supply it, and how it should be spent are secondary to this. . . .

There is need for the development of a very strong Committee on Research, with representation from all areas—socioeconomic, legal, and educational, as well as scientific. . . .

The A. M. A. has not yet assumed leadership in atomic medicine and ionizing radiation, electronics, and other areas of physics which open

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tant to the advancement of American medicine than is a "Public Relations" program?

—Should the A. M. A. develop appropriate standards to combat misleading advertising? Should it conduct a "consumers' research" type of program for medical instruments, devices, and apparatus intended for use by the physician only?

Those and other questions rang out at the opening session, echoed in group discussions, reverberated at the ad hoc committee session, and still sounded as the conference was closing. Some, of course, were asked more in broad challenge than in specific search. Others await answer in studious deliberation. "The report of this meeting," said Dr. Hugh H. Hussey, the conference chairman, "will be subject to careful review. We may expect the beginning of some changes. This will require sifting, enlargement, and development. Out of House of Delegates actions, programs then will arise."

When the conference ended, that statement was providing the soundest reply to the question, "What, specifically, happened at Hershey to change things?" What happened was that for the first time in A. M. A.'s 113-year history wise men not only assembled humbly but also examined fearlessly and projected hopefully. What happened was impetus.

"This has been a revolutionary occasion," says Dr. Millis, "a revolutionary occasion on which we were trying to see how revolutionary forces might be channeled to produce evolutionary change."

Members of the Committee on Scientific Activities of the A. M. A. Board of Trustees are Drs. Julian P. Price of Florence, S. C.; Rufus B. Robins of Camden, Ark., and Hugh H. Hussey of Washington, D. C., Chairman.

"A Little More ....

As physicians become more effective are their patients, individually and collectively, becoming more perverse? Leo W. Simmons, Ph.D., professor of sociology at Yale University and one of about 65 American sociologists specializing in the field of medicine, asks that question. He told physicians and other participants at the A. M. A. scientific assessment conference in Hershey, Pa.:

"There's not much difference between us under the skin. We [medical scientists and sociologists] are really brothers. You already have in your bag of knowledge tremendous therapeutic potential which society is not allowing you to use—through

.... *Help Shape Medical Science Tomorrow?*

new pathways to the understanding of normal physiological and many pathological processes. By this time, the A. M. A. should have established the mechanism for collecting, analyzing, and screening new knowledge in this field and for properly communicating its medical implications to the profession and to the public. . . .

On specialization—

The proper function of the specialty boards is the examination of candidates for membership. Boards go beyond their prerogative when they specify a too rigid educational program to achieve those ends. . . .

Medicine is fragmented by specialization, and specialization is an absolute necessity. We will have more of it and it shall be more intense as the physician tries to multiply his effectiveness. . . .

Modern medicine is just beginning to discover that it takes just as much effort to achieve cooperation between specialists as it does to achieve specialization itself. There is the great lag: keeping pace with specialization through cooperation between the specialties. They [specialization and cooperation] go together. . . .

On communications—

There is the important problem of coordinating the educational work of the Councils and Committees within the A. M. A. Communication is inadequate; there is not even a central clearing point for its many educational activities. . . .

The A. M. A. could make a real contribution by developing a field service for scientific activities—to disseminate ideas, suggest guest speakers, provide technical assistance—helping medical societies develop scientific programs and postgraduate educational activities. . . .

On unity—

If we adopt the easy way of meeting problems, by organization of one more Division or one more Council, as a universal technique, then we are introducing additional divisive forces and are not doing what the A. M. A. wishes to do—provide unifying devices. . . .

There is a conflict between physicians and other medical scientists. It is real and is hurting the progress of medicine. It is reflected socially, economically, and in work patterns. One suggestion is to modify the salary scales so that people are paid for what they do and what they are worth, regardless of the degree they hold. . . .

On ideas for the future—

A medical science group directly advisory to the Board of Trustees could open an avenue along which the hopes and aspirations, the goals and the desires and the dreams of the medical scientist—the essence of the thing that makes him tick—could be communicated directly to a top responsible body of the Association. . . .

Activities of a reorganized Division of Scientific Activities might be arranged under four headings dealing with permanent and basic questions of instrumentation, measurement, assessment, and communication. That could compose the framework. Most problems in medicine are, in the broad view, temporary ones which can be handled in such a framework and in ad hoc committees drawn from within those four headings in the organization as well as from outside the Association. . . .

What's Ahead in Legislation? A. M. A. Session Seeks Answer

Two U. S. congressmen, a state governor, a leader in public health, and a farm group executive have joined with representatives of medicine to offer an integrated view of what lies ahead in legislation affecting the public and the medical profession.

They were among 240 registrants at a Medical Legislative Conference held Oct. 2 and 3 in St. Louis under the auspices of the A. M. A. Council on Legislative Activities. Most of those who took part in the discussions, which related to the health of the aged, were physicians and executive secretaries from 49 state medical associations (only Alaska was not represented). Participating also were three members of the A. M. A. Board of Trustees, several officers and past-presidents of the A. M. A., and top executives of the headquarters staff.

Presentations were delivered by Governor Robert E. Smylie of Idaho, U. S. Representative Thomas B. Curtis from Missouri, U. S. Representative Dale Alford, M.D., from Arkansas, executive director Ben Read of the Public Health League of California, and Roger Fleming, secretary-treasurer of the American Farm Bureau Federation. Said Dr. George M. Fister, the Council chairman who presided at the conference, "Activities in Congress dealing with health care for elderly people need careful examination by all elements and at every level of our society, so that medicine's constructive role can be understood more clearly as it benefits the public at large."

.... *Penicillin, Please. . . ."*

public apathy, opposition, and other barriers. That is the paradox: A doctor can see people around him sick and dying—and know what to do, but sometimes not be allowed to do it because of these barriers.

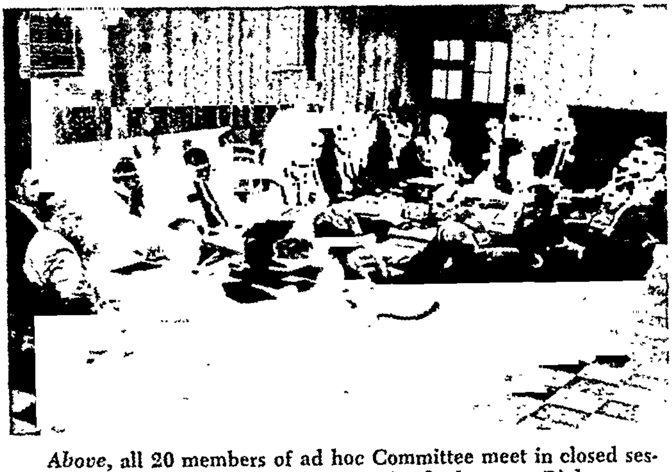
"At the same time you are confronted with an increasingly sophisticated clientele of patients, and they are becoming more and more critical of medicine—'A little more penicillin, please, doctor.' And sweeping commercialism is forcing much of the public to look at the doctor as someone who has some special skill to sell—yes, to sell."

Scenes from Hershey Conference

Growth and influence of specialty boards are discussed at a group conference in Hershey, Pa., during historical review of A. M. A. scientific activities.

Group conference on important issues in behavioral sciences is chaired by sociologist Leo Simmons, *left*. Three-day session opened Sept. 14.

Left, session begins for 79 participants, including members of A. M. A. Board of Trustees, staff executives and ad hoc Committee members. *Above*, another of five conference groups examines aspects of formal medical education.



Above, all 20 members of ad hoc Committee meet in closed session to summarize findings of groups for final report. *Right*, scene at plenary session.

They Run, Jump, and Throw Under The Watchful Eye of Medicine

While athletes from 35 countries sprinted around tracks, hurled the shot, raced on bicycles, and boxed one another in September's Pan American Games in Chicago, their physicians, trainers, and physical educators were meeting to consider the physiological problems that result from such strenuous activities.

The 200 who registered for the third Pan American Sports Medicine Congress heard speakers discuss such diverse topics as research in athletic injuries and the effects of altitude on performance:

–The prevention of athletic injuries has only recently begun to receive the attention it deserves, according to Dr. Allan J. Ryan, Chairman of the A. M. A. Committee on the Medical Aspects of Athletics. He told the Congress, "In the vast field of medical publications there has been until just recently a remarkably scanty list of authoritative articles and books to which the newcomer to this field could turn for guidance. . . . As a consequence, this field of sports injuries has been one of the last strongholds of empiricism in medical treatment." A quickening interest in this field is indicated by the fact that the A. M. A. will sponsor a national conference on the subject this month in Dallas, Texas, prior to the Clinical Meeting.

–Changes in altitude, according to Dr. Peter Karpovich, research professor of physiology at Springfield College in Massachusetts, can have a distinct effect on athletic performance if the subject trains near sea level and then is called on to perform at a higher altitude. Dr. Karpovich noted that visiting athletes competing in the 1955 games at Mexico City's 7,500-ft. altitude turned in significantly poorer performances there than they had in other contests. Five of 6 discus throwers tested seemingly were affected, as were 12 of 13 swimmers. Periods allowed for acclimatization of those making the poorer showings had usually been very short.

While Chicago's low altitude probably did not affect the visiting athletes this year, the atmosphere may have. The city laid on a record wave of heat and humidity.

"We don't have weather like this where I come from," one athlete from a semitropical country complained to Mayor Richard Daley. "You should have come when the Queen was here," the Mayor replied. "The weather was splendid then."

Executive committee members discuss first draft of reference work on homemaker services.

Out of a Conference–A Primer For Homemaker Services

When the word "Homemakers" is capitalized, it refers to the nearly 2,000 women at work in the United States today helping troubled families. Recruited, trained, and supervised by voluntary agencies and departments of public welfare, these women are assigned to families temporarily deprived of the services and stabilizing influence of the wife and mother.

But 2,000 are not nearly enough, and those who concern themselves with such things are working hard to stimulate the expansion of such services. One group, perhaps more concerned than any other, is the Executive Committee of the National Conference on Homemaker Services which includes representatives of the A.M.A. and 25 other organizations interested in the health and welfare of Americans. Meeting in New York last September, the committee plunged into its current task of compiling a volume on the history, need, and methods of establishment of homemaker services. When it is completed next spring, the 300-page encyclopedia is expected to serve as a primary source of homemaker information.

The volume is being based on material and recommendations produced by the 400 physicians, welfare workers, nurses, insurance executives, labor officials, and lawyers who attended the two-day Homemaker Conference held in Chicago last spring (see Medicine at Work, The Journal, March 21, 1959).

The increasing demand for homemaker services does not stem entirely from the lower income groups. The need for such a service may be just as urgent in a family which can afford to pay for such help but cannot find it. This dilemma was noted by Dr. David E. Price speaking at the national conference. He said, "There is a great deal of difference between trying to hire a maid, hoping that she will stay in spite of difficulties and health emergencies in a family, . . . and welcoming a trained person coming into the home because of these very difficulties and disruptions."

They Bridge the Gap Between Self-Care and the Institution

Richard P. Pratt

Mrs. Rogers is afraid. Living in the second largest city in the world, she is alone. Widowed and childless, she has lived for the past eight years in a tiny rented room, comforted only by her few remaining possessions. Now, failing eyesight has made even her little shopping trips a misery and cooking a chore. Proud, but with a pride tinged with realism, she faces the necessity of changing her mode of living. . . . Change. . . . Even the word creates apprehension. If only she had a family she could turn to. . . .

In some of our larger cities today—and in some of the smaller ones, too—there is a family for Mrs. Rogers, and other families for other elderly persons in similar circumstances. Families willing to share their homes, their food, their small pleasures, and perhaps even some of their burdens. They are members of what are variously called foster home plans for the aged, substitute family plans, or residential placement programs. They are families willing to provide not only bed and board but some of the companionship, warmth, and personal contact so necessary to human happiness.

Some of these programs are offered by welfare agencies, others by voluntary social service groups, but, whatever the sponsorship, they are providing an alternative living arrangement for the aged that lies between self-care and an institution. Foster home plans for the aged are a modification of the foster home theory long used to good effect in caring for children deprived of parental support. In both, the underlying philosophy is the same—that, where possible, life in a small household is preferable to life in an institution.

The recruitment of potential foster homes is one of the problems facing any organized program of substitute family care for the elderly. Newspaper advertisements, talks before civic groups, personal referrals, and appeals through religious groups are the usual channels, although the imaginative approach also pays off. In Baltimore, an agency fattened its list with prospects who had applied for foster children but had failed to make the grade. One in Brooklyn accepted client referrals from religious groups, with a request that each group locate another home to add to the roster.

Once found, the home must measure up to a check list of standards. Most agencies require that the client be given a private room, furnished with linen, allowed use of the telephone, permitted visitors and reasonable use of the living room, and provided with appetizing food. Initial interviews with the family and inspection of the home are necessary, and continuing agency supervision is deemed advisable.

Family Matchmaking

Once a list of suitable homes is compiled, the agency's real work begins. Probably no element of the plan is more crucial to its success than the matching of client with his prospective host. Miss Ruth M. Snyder, assistant to the director of special services of the New York City Department of Welfare, says, "A good matching job requires patience, understanding, and skill and depends on a knowledge of the home and the proprietor as well as the prospective boarder's health and personal needs, interests, and eccentricities."

However skillfully the two have been prematched by the agency, the proof of the pudding is their first meeting. The Jewish Community Services of Long Island explains its method this way: "On the day of the meeting, both persons are seen first by the worker and then introduced to each other. They are given an opportunity to talk to each other alone, and both can discuss what they have to give each other, the arrangements, etc. After this meeting, both clients are again seen briefly by the worker for their initial reactions." Providing such a beginning is successful, the client then visits the home, takes a look at the surroundings, and prepares himself for the move.

Smoothly functioning in the background of such work are the medical skills of interested physicians. Physical examination of boarders prior to admittance is considered a necessity, and at least one agency requires that a physician certify the homeowner's fitness to assume the added burden of care that taking in a boarder will mean. Doctors are often consulted, too, about special physical and dietary problems, as well as continuing medical care. Among the voluntary agencies, physicians' names are prominent in lists of directors. One agency even goes so far as to seek psychiatric evaluation in cases in which the prospective boarder has an emotional problem.

Payments and Personals

Payments for foster home care come either from the private funds of the boarder or from welfare agencies, or both. Costs range from $100 to $150 per month, depending on regional area, services provided, and other factors. While financial profit is considered an acceptable motive for wishing to

Feeling of a Family

"We place major emphasis on the 'home' aspects of the program. Our concern goes further than just finding a room for our client-boarder to rent and occupy. Although we do not expect him (or her) to be adopted by the proprietor, we do like to know that he is living in a home where he can have the feeling that he belongs to a family."

—Booklet offered to owners of prospective foster homes.

have foster members in a family, agencies generally require that the family have an income of its own in addition to such payments. Whatever the original financial incentive, foster families often find themselves caught up in the interpersonal relationships that such placement inevitably generates. In New York City, the foster home program of the Department of Welfare sends a quarterly newsletter to all foster families on its list. The newsletter contains a variety of material, but it is in the "personals" that the value of the foster family concept shines through:

—"Bouquets to Mrs. P. . . . who has earned the affection and gratitude of Mr. B. . . . for many kindnesses, not the least of which is encouraging him to resume playing his violin. He is a former concert violinist."

—"Mrs. H. . . . has many times told us of her thankfulness for the understanding care she receives from Mrs. D. . . . She has an unusual handicap which has affected her speech and Mrs. D. . . . has been very resourceful in finding ways to communicate to avoid frustrations."

—"There was a gala birthday celebration at the M. . . . home for the 90th birthday of Mrs. A. . . ., with about 20 guests present. There were gifts and flowers, and the party dress worn by Mrs. A. . . . was the prettiest of all."

Often, of course, the foster home is not the final residence of the elderly person. Increasing age, incapacity, or burdensome illness sometimes makes removal to a hospital or nursing home advisable, but, as Miss Snyder points out, such decisions are not easily made. She writes:

"The line of demarcation between the need for nursing care and the care provided in a boarding home is sometimes very tenuous. We ourselves are not always sure, and frequently the attending physician makes a strong plea that the client stay where she is rather than be moved, *insisting* that nursing care is not needed. In many instances, [families] have become so attached to their elderly charges that they are not only willing but eager to keep them, despite limitations of health and deteriorating personality."

Two-Way Street

Agencies operating foster home programs have become increasingly aware that they are doing more than just finding a home for an elderly client. William Posner, assistant director of the Jewish Community Services of Long Island, states, "In the process of matching resident and family, we have become convinced that it works best if the family needs an older person as well as the other way around. The older person can become a real companion to a foster family. In recent years, we have been recruiting more and more younger families in whose home the older person becomes a grandparent figure."

A slightly different view of foster home plan usage is visualized by Maurice J. Ostomel, executive director of the Jewish Home for the Aged of Los Angeles, which hopes to develop such a program as part of its master plan. Mr. Ostomel notes that such homes can provide temporary care, for persons on the waiting lists of homes for the aged and also for the short-term placement of the elderly when those who have been caring for them are called away, hospitalized, or otherwise burdened. He states, "A foster home placement service can serve as a valuable part of the armamentarium of a home for the aged."

One telling indication of the relationships that arise between families and their elderly guests was illustrated last summer at a small ceremony held by the New York Department of Welfare to honor ten of its foster home owners who had given a decade or more to the program. Nine of the guests of honor were present to receive the small gold pins the department was awarding. The tenth failed to appear. She was too busy nursing an elderly guest who had suddenly fallen ill.

A Friendly Face

"During the last years, we have surrounded foster care with a variety of adjuncts, the most important being friendly visiting services," says William Posner, assistant director of the Jewish Community Services of Long Island, N. Y., a pioneer in the substitute family field.

He adds, "We have found that many people—in addition to family living—require the personal interests of 'outsiders.' These friendly visitors bring the outside world in, and this is particularly important where the older person has no relatives of his own."

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THE HERSHEY CONFERENCE

"He that will not apply new remedies
must expect new evils"—Bacon

The conference in September at Hershey, Pa., under the auspices of the A. M. A. Board of Trustees' Committee on Scientific Activities was a unique and rewarding experience, the positive value of which it is anticipated will become appreciable during the period ahead.

The conference was developed around a group of 20 invited *ad hoc* advisers from the field of medicine and allied scientific areas, each selected for outstanding competence in his or her area of scientific interest. Others in attendance included members of the A. M. A. Board of Trustees, executive officers, and division directors, together with the responsible administrative personnel and representatives of each of the councils and committees within the division of scientific activities. Résumé background material concerning past, current, and projected activities of the division had been studied by all participants well in advance of the meeting. The entire conference was conducted in the spirit of invitation and challenge to use reason and thought in searching for the solution to current and future needs and problems.

The ideas and suggestions resulting from the two and one-half-day conference were eloquently summarized at the final session by President John S. Millis of Western Reserve University. If the American Medical Association is to effectively play its role as the greatest single force in American medicine to counteract the divisive forces within medicine itself, it must be the pivotal factor in producing coherence and unity. In addition to this sound counsel, five central ideas relevant to thinking and action were proposed by the conferees for the American Medical Association.

The first of these dealt with people for medicine through the role the American Medical Association should play in the assurance of enough of the right kind of people for the continuance of the profession. The Association should have deep concern and interest regarding the number, quality, and recruitment of medical students, as well as in the development of adequate facilities, faculties, and financial support to insure the education and training of sufficient medical personnel in the period ahead. It should also be concerned with the need for sufficient numbers of practitioners in the various fields to render good medical care. The American medical profession should be vitally interested and concerned with what might be termed the "seed corn," namely those members of the profession who serve as the teachers and investigators. Furthermore, there is a direct challenge for communication from organized medicine to the young people of America, and to the public in general, about the people of medicine, as well as the challenges it presents today .

Secondly, education for medicine has become a fragmented responsibility. Education, in general, covers a vast sweep, of which medical education is just a part. Today we cannot think in isolation but must think and plan in terms of a continuous process of education for medicine. If medicine, and the American Medical Association in particular, is concerned only about medical education, it is blind indeed. It must be just as vitally concerned today with chemistry, biology, sociology, physics, psychiatry, and other areas as with education leading directly to qualification in clinical fields. Full realization and effective utilization of this comprehensive approach constitutes one of today's outstanding scientific and educational challenges.

The third area of concern dealt with interprofessional and intergroup relations. Medicine itself is fragmented and may be even more so in the period ahead. Physicians will need the assistance of more and more persons in allied fields. Consequently, the relation of medicine to the areas and groups allied to it becomes increasingly important. The American Medical Association must take a positive approach in this area, and it should take leadership to invite appropriate interprofessional and intergroup cooperation. It is gratifying to note that real efforts have been under way in this direction during the past two years. One valuable positive approach might be through the establishment of a group of such scientists to serve in an advisory capacity to the Board of Trustees.

inquiry for medicine constituted the fourth suggestion. The conference group emphasized that the conduct of research activities involves an area in which many other agencies (such as universities and institutes) can do certain types of studies more effectively than the American Medical Association. However, the conferees believed it exceedingly important for the American Medical Association to have the appropriate mechanism for reviewing research, identifying and filling gaps, and undertaking direct inquiry in certain areas, as, for example, those dealing with standards of medical care. What is adequate medical care is by no means an appropriately answered question. The American Medical Association should also measure the desires and needs of practicing physicians in regard to continuing medical education. Its headquarters staff should constantly play a role in evaluative functions involving the distillation of wisdom from information and its subsequent appropriate communication. Fundamental is the constant effort to communicate and transmit ideas, thought, and wisdom so that they may be effectively utilized.

And finally, the philosophy of organization for medicine in its scientific and other efforts was emphasized. Since the American Medical Association is, and should be, a unifying force, it must be careful not to be divisive in its organizational techniques. In the past the Association has tended to develop new councils, committees, or bureaus whenever a special problem has arisen. Over the years this mechanism has tended to become divisive and should be carefully reevaluated. The American Medical Association should organize its total responsibility so that the organization integrates all of these elements.

It will be a year or so before the impact of the Hershey conference can be fully evaluated. It pointed up many suggestions that will undoubtedly play an important role in projecting the scientific activities of the American Medical Association during the period ahead. It has clearly indicated the innumerable ramifications of the concern of the division of scientific activities with the problems and interests of all other divisions. Effective planning and action during the period ahead, therefore, necessitates that those responsible think, plan, and work in terms of the American Medical Association as a whole, that perspectives be broad, and that this great voluntary association and its staff constantly strive toward coherence and unity in their efforts.

(A Medicine At Work pictorial-and-text report on the Hershey Conference appears on pages 1699 to 1702.)

ORGANIZATION SECTION

NATIONAL CONFERENCE ON THE MEDICAL ASPECTS OF SPORTS

The program for this conference, sponsored by the American Medical Association for physicians, athletic directors, coaches, and trainers, which meets at the Baker Hotel, Dallas, Texas, Nov. 30, 1959, immediately preceding the A. M. A. Clinical Meeting, Dec. 1-4, is as follows:

Morning

8:00 Registration

9:00 First General Session, *Ballroom*
Presiding: Allan J. Ryan, M.D., Chairman, Committee on the Medical Aspects of Sports, American Medical Association.
Greetings from the Association: Louis M. Orr, M.D., President, American Medical Association.

9:30 Divided Sessions
Section I: **Physiology of Exercise,** *Texas Room*
Presiding: David J. Henry, M.D.
The Biodynamic Potential of the American Male Population.
Bruno Balke, M.D.
Oxygen Debt in Near-Anaerobic Exercise.
David B. Dill, Ph.D.
Amphetamine Sulfate and Athletic Performance: II. Subjective Responses.
Henry K. Beecher, M.D.
Exercise and the Kidney.
Warren R. Guild, M.D.
Section II: **Prevention of Athletic Injury,** *English Room*
Presiding: Owen B. Murphy, M.D.
A Medical Program for High School Football.
Joseph H. Burnett, M.D.
Panel Discussion: **Protective Headgear for Athletics, Research and Development.**
Chairman: Henry J. Montoye, Ph.D.
Creighton J. Hale, Ph.D.
Alexius Rachun, M.D.
George G. Snively, M.D.

11:15 General Summary Session, *Ballroom*.
Summary for Divided Section I,
David J. Henry, M.D.
Summary for Divided Section II,
Owen B. Murphy, M.D.
Questions, Comments, Discussion

Afternoon

12:15 Luncheon Meeting (tickets available at registration desk), *Terrace Room*
Presiding: ALLAN J. RYAN, M.D.
Youth Fitness Today.
MR. HOMER C. WADSWORTH, Chairman *of the President's Citizens Advisory* Committee on the Fitness of American Youth

2:00 Divided Sessions
Section III: **Training and Conditioning the Athlete**, *Texas Room*
Presiding: EDWARD T. SMITH, M.D.
The National Athletic Trainers' Association and Its Program.
MR. WILLIAM E. NEWELL
Effort and Fatigue in Athletics.
J. KENNETH DOHERTY, PH.D.
The Role of Physical Conditioning in Prevention of Athletic Injury.
HANS KRAUS, M.D.
Section IV: **Treatment of Athletic Injury**, *English Room*
Presiding: AUGUSTUS THORNDIKE, M.D.
The Pathology of Trauma.
RICHARD PATTON, M.D.
Panel Discussion: **The On-Field Duties of the Team Physician.**
Chairman: CARL E. BADGLEY, M.D.
WILLIAM D. PAUL, M.D.
FRANCIS MURPHEY, M.D.
THOMAS B. QUIGLEY, M.D.

4:00 General Summary Session, *Ballroom*
Summary for Divided Section III,
EDWARD T. SMITH, M.D.
Summary for Divided Section IV,
AUGUSTUS THORNDIKE, M.D.
Questions, Comments, Discussion

Evening

8:00 Evening General Session, *Ballroom*
Presiding: ALLAN J. RYAN, M.D.
Introduction of Guests
The Modern Olympic Games (*movies of 1956 Olympic Games to be shown*).
MR. AVERY BRUNDAGE

THE SMALL MEDICAL LIBRARY

The A. M. A. Library has prepared a pamphlet, "Recent Books and Periodicals Selected for the Small Medical Library." Copies may be requested from the library.

GOVERNMENT SERVICES

FOOD AND DRUG ADMINISTRATION

Court Actions in September.—Insect contamination and live infestations were found in shelled peanuts, flour, egg noodles, rice, prepared baking mixes, and a breakfast cereal. Spoilage was found in salad dressing and in seafoods, including fillets of cod and perch and frozen lobster tails. Of the remaining unfit foods seized, 55 tons were in insect-infested peanuts and pistachios, and 49 tons in rodent and insect-contaminated wheat, rice, flour, and corn meal. Ten tons of tomato paste contained fly eggs and maggots and were alleged to have been prepared and packed under insanitary conditions. Seven tons of dried blackeyed peas were insect infested.

Seized as economic cheats were 3.5 tons of imported cocoa powder in which cocoa shell was substituted for cocoa, an instant coffee containing dextrose in place of coffee, "chocolate" fudge cookies made with cocoa rather than chocolate, canned peaches labeled as "irregular slices in heavy syrup" that were actually irregular sizes and shapes in light syrup, and short volume cans of salad and cooking oils.

Of 24 drugs and devices seized, 16 were alleged to be misbranded by false and misleading claims. Five shipments of a so-called "breast developer" were seized at Tampa and Clearwater, Fla. The action filed in the federal district court charges that this device will not increase the size of a woman's breast and that it is a hazard to health as well as a fraud. Mineral bath salts were offered at $9.95 for a 3-lb. package to treat objectionable body odor, brighten the eyes, and build up resistance to disease. Two makes of canister-type vacuum cleaners were offered as preventives of such "airborne" infections as boils, abscesses, bone infections, "strep" throats, scarlet fever, tonsillitis, tuberculosis, pneumonia, influenza, and the common cold. Another so-called air purifier consisted of a cabinet-enclosed fan, nylon filter, and two ultraviolet ray tubes. Air drawn in by the fan was passed over the tubes, allegedly "ionized," and then recirculated. The device was offered for relieving allergies, asthma, coughs, sinus trouble, colds, and virus infections and for reducing the spread of airborne disease germs.

Wooden Ball Weight Reducer Seized.—From northern India, where all women allegedly have slim figures, came a 1,000-year-old reducing device that allegedly had been tested and proved by the women of Paris. It is small enough to fit conveniently in a handbag, weighs only 11 oz., consists of 10 wooden balls that rotate in a plastic frame as the balls are rolled over various areas of the body, and costs $10.

About 15,380 of these were seized as being misbranded by false and misleading claims for reducing weight; reproportioning the entire body; stimulating the tissue to circulate fresh lively blood; eliminating fatigue; banishing constipation, headache, a sallow complexion, and rheumatic ailments; eliminating toxins that poison the bloodstream; and preventing premature aging.

Caffeine Promoted as a Vitamin.—"Dynamol," the featured ingredient of a vitamin product claimed to pep you up in 20 minutes, was found to be caffeine; 37,800 tablets were seized as misbranded by false and misleading claims. The promoter claimed that the product contained a "new, remarkable, amazing, antifatigue factor" and, because it contained "Dynamol," was superior to all other vitamin-mineral preparations. "One tablet per day," he said, "is an adequate cure and treatment for all vitamin and mineral deficiencies." The product did not contain any vitamin A or D and contained only insignificant amounts of calcium and phosphorus.

Illegal Sale of Drugs.—Two decisions by the United States Court of Appeals for the fifth circuit upheld the convictions of Dr. Samuel J. DeFreese and Marsha Jean Simmons DeFreese, his wife, of Monroe, Ga., for selling large quantities of amphetamine sulfate, a drug that can legally be sold only by prescription, to truck drivers. In one decision, the circuit court upheld the government's proof of identity of the tablets and the fact that they came from an out-of-state manufacturer. This evidence came from an FDA microanalyst who identified the tablets by means of punch marks and other microscopic findings. In the second opinion, the court rejected the contention of Dr. and Mrs. DeFreese that the federal pure food and drug law regarding the sale of prescription drugs applied only to sales at the retail or pharmacist's level. The court held that the law applied to bulk sales for resale by a physician—in this case the sale of 5,000 and 10,000-tablet quantities to federal inspectors who posed as truck drivers who wanted them for resale to other drivers.

"Wonderpad" Found Worthless.—An old-fashioned fake medicine pitch was made by a Jackson, Pa., mail order promoter of so-called "radioactive" mittens and pads as a cure for arthritis, rheumatism, bursitis, neuritis, swellings, stiffness and soreness of the joints, and similar conditions. His "Wonderpad" did not contain uranium or any other radioactive material but was filled with chunks of rock and pulverized dirt. The mittens sold for $12 and pads for $22.

Defendant in Food Poisoning Case Sentenced.—Daniel DiOrio, president and treasurer of the Universal Sea Food Co., Inc., Philadelphia, pleaded guilty on Sept. 21 to charges of adding sodium nitrite to flounder fillets with intent to mislead and defraud. He was indicted after an investigation of a major food poisoning outbreak, including the death of a child, in the Philadelphia area last spring, and was sentenced to one year in jail and a fine of $2,000. Eleven months of the jail sentence were suspended and the defendant placed on probation for three years. The sea food corporation, which went out of business as a result of the food poisoning incident and publicity, was fined $100.

Counterfeiters of Tranquilizer Drugs Sentenced.—Two drug counterfeiters were convicted and sentenced on charges of conspiracy with intent to defraud and mislead. They used the facilities of a legitimate drug manufacturer after regular working hours to reproduce the size, shape, grooves, and distinctive monograms of the tablets of two well-known brands of tranquilizer drugs. Like the genuine article in appearance only, the counterfeits were substantially lower in the strength of the active drug ingredient. Ludwig Spandau, of New York City, was found guilty on seven counts involving manufacture and interstate sale of the counterfeit tablets and was sentenced to six months in jail on each count, with the sentences to run concurrently. The sentence was suspended and Spandau was placed on probation for one year. Seymour Blau, who conspired with Spandau, pleaded guilty to five counts and testified for the government against Spandau. He was fined $50 on each of four counts and placed on probation for one day.

Voluntary Corrective Actions.—Nineteen individual plant improvements costing $41,167 were made voluntarily by food manufacturers and warehousemen in September to assure the production of clean, wholesome products. In an additional 102 voluntary actions to protect consumers, food firms destroyed or converted to nonfood uses 233 tons of unfit foods. A California frozen pie company spent $5,000 to prevent possible bacterial contamination of its product. The firm bought two portable sanitary pumps to transfer materials, formerly handled with buckets, and improved its freezing method to cut down the incubation period for possible bacterial growth. A Michigan bakery supplier avoided possible insect and rodent contamination of warehoused products by storing them on newly acquired pallets for handling by fork lift and installing new floor covering. A Colorado candy manufacturer shut down his plant for one week for a complete clean-up and repainting. Practically all the dollar value of substandard drugs voluntarily destroyed by drug firms was in a single action by a California manufacturer of a wetting solution for use with contact lenses. Finding the product was not sterile, the manufacturer voluntarily recalled from the market and destroyed stocks valued at $167,000.

MEDICAL NEWS

ARKANSAS

Plan Germ-Free Laboratory.—Dr. Jerome J. Landy, assistant professor of surgery at the University of Arkansas Medical Center, Little Rock, received a $222,790 grant from the National Institutes of Health, U. S. Public Health Service, to establish a germ-free laboratory for research in surgical problems. The grant is to finance the project for the next five years. There are only five major germ-free laboratories in the world, one in Sweden, one in Japan, and three in the United States. The major laboratories in this country are located at the University of Notre Dame, Walter Reed Army Research Institute in Washington, D. C., and the National Institutes of Health in Bethesda, Md. In his laboratory to be established in the Medical Center's new Barton Institute for Medical Research, Dr. Landy will use germ-free animals, and the initial study will be on the role of bacterial toxins in intestinal obstructions. The animals will be studied while they remain free from bacteria and then will be studied with added and controlled bacterial populations.

CALIFORNIA

Plan Concert by Doctor's Orchestra.—The Los Angeles Doctor's Symphony Orchestra announced that Leon Arnaud, doctor of music, will be guest conductor for the orchestra's concert Jan. 23, 1960, in the Philharmonic Auditorium. Dr. Arnaud recently was conductor of the Madrid Symphony Orchestra in Spain. The Doctor's Symphony Orchestra also announced that the Reiss-Davis Clinic will be the beneficiary for the concert. Physicians who wish to play with the orchestra are asked to call Dr. Lester M. Morrison, president, at Olive 3-7080 or Dr. Milton Lane at Pleasant 3-2505.

University News.—Dr. Maxwell S. Jones, director of the social rehabilitation unit at Belmont Hospital, Surrey, England, joined the Stanford Medical School staff in July. A practicing psychiatrist since 1932, Dr. Jones will be at Stanford for a year's visit. During 1950-1951, he was a consultant to the World Health Organization at Geneva.——Appointment of Dr. Edward R. Pinckney, of Beverly Hills, to a newly created position at the College of Medical Evangelists School of Medicine was announced. Dr. Pinckney will serve as executive director of CME's new Audiovisual Postgraduate Extension Courses in Medicine.

Medical Library in San Francisco.—The opening of the new Medical Library at San Francisco-Stanford Hospital was celebrated Oct. 30, with a reception for San Francisco physicians, staff members, and emeritus professors from the Stanford University School of Medicine. Dr. Emile F. Holman, Dr. Arthur L. Bloomfield, Dr. Robert R. Newell, Dr. Ludwig A. Emge, and Dr. Harold K. Faber were present to encourage the new collection. To commemorate the event, Dr. Hans Barkan, emeritus professor of ophthalmology, donated an autographed copy of his book, "Johannes Brahms and Theodor Billroth: Letters from a Musical Friendship." Many of those present remembered a day in 1901 when Dr. Emmet L. Rixford established the central core of Lane Library with his gift of 30,000 medical volumes obtained from the New York Academy of Medicine and the New York Hospital Libraries. The Lane Library is now located on the Stanford University campus in Palo Alto. The library has more than six hundred standard texts on medicine, surgery, radiology, and related fields. One-third of the texts are newly purchased and gifts of books and private medical libraries are added daily.

ILLINOIS

Dr. Press Named Health Director.—Dr. Edward Press, field director, American Public Health Association since Jan. 1, 1955, has become the public health director for Evanston. He succeeds Dr. Winston H. Tucker, who died a year ago.

Chicago

Dr. Lundy Comes to Chicago.—Dr. John Silas Lundy, founder of the section of anesthesiology of the Mayo Clinic, Rochester, Minn., in 1924 retired Oct. 1 and will continue the private practice of his specialty in Chicago.

Foreign Lecturer.—Rudi Borth, Ph.D., lecturer in hormone assay, head of the Endocrine Laboratory, University Clinic of Obstetrics and Gynecology, Geneva, Switzerland, presented "Gonadotrophic and Steroid Assays in Normal and Disturbed Pregnancy" Nov. 4 at The Chicago Lying-in Hospital, The University of Chicago School of Medicine.

Dr. O'Conor Gives Annual Lecture.—Dr. Vincent J. O'Conor, professor of urology and chairman of the department, Northwestern University Medical School and Chicago Wesley Memorial Hospital, gave the annual Belfield Lecture to the Chicago Urological Society, Nov. 4. His subject was "Surgical Correction of Male Sterility."

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Dr. Holinger Receives Medical Photography Award.—The Louis Schmidt Award of the Biological Photographic Association was awarded to Dr. Paul H. Holinger at the annual meeting of the association in Montreal Sept. 3. The award is named for one of the leaders in medical illustration who was a pioneer in the use of photography. Dr. Holinger was named the recipient "for outstanding contributions to the progress of biologic and medical photography, particularly for his work in endoscopic still and motion picture photography." He is the first physician to receive the award.

Plan New Medical Center.—Loyola University reaffirmed its intention of constructing a multimillion dollar medical center on its 54-acre site in northwest Chicago and described its plans for coping with the expanding operational costs of the Stritch School of Medicine. The Very Rev. James F. Maguire, S.J., university president, revealed that Loyola will form a board of lay trustees to finance, build, and operate a teaching hospital for the university medical school on its site near southwest Skokie. About 3 million dollars in addition to those funds already received for that purpose will guarantee the construction of a teaching hospital.

Lectureship Award to Dr. Katz.—Albany Medical College presented its third annual honorary lectureship award to Dr. Louis N. Katz, director of the cardiovascular department, Medical Research Institute, Michael Reese Hospital, and professional lecturer in physiology, University of Chicago, at ceremonies held at the Medical College Nov. 19. His lecture was entitled "Energetics of the Contracting Heart." The lectureship award consists of an inscribed plaque and honorarium. It is given in recognition of "distinguished service to mankind in the fields of science, medicine, and teaching."

IOWA

Dedicate Steindler Library.—A library established in memory of the late Dr. Arthur Steindler was dedicated Nov. 1 in the department of orthopedic surgery at the State University of Iowa, Iowa City. Dr. Steindler died last July at his Iowa City home at the age of 81. Dr. Carroll B. Larson, Dr. Steindler's successor as head of the university's department of orthopedics, said that more than 1,000 volumes from Dr. Steindler's personal collection of books will be placed in the memorial library, located in the east wing of Children's Hospital in a room formerly used as a study area for resident physicians.

KANSAS

Report on Rabies.—A case of rabies in a civet cat was confirmed recently in Butler county. The antirabies treatment was administered to a 25-year-old housewife who had been bitten by the animal. A six-year-old Russell county boy was reported to have been bitten on the hand and face by a bat, while playing in a barn. Unfortunately, a cat caught and ate the bat. Attempts to catch other bats in the barn were fruitless. The child was given a complete series of the duck-embryo vaccine. The Public Health Service warns that rabies-infected bats "may not exhibit Negri bodies nor harbor the virus in the brain, even though the virus is present in the salivary glands." This applies to infected bats whether or not they show symptoms of rabies.

MARYLAND

Create Soper Lectureship.—Friends and colleagues of Dr. Fred L. Soper, Washington, D. C., on his election as the director emeritus of the Pan American Sanitary Bureau, Regional Office of the World Health Organization for the Americas, and on his relinquishing the active direction of that program, created a lectureship in his honor. This lectureship will provide for at least an annual lecture in one of the schools of public health throughout the world. The first Fred L. Soper lecture was given by Dr. Soper himself at the Johns Hopkins School of Public Health, Baltimore, his alma mater, Oct. 27 on the subject, "The Eradication Concept in World Health."

Personal.—Lorin J. Mullins, Ph.D., on leave of absence as associate professor of biophysics at Purdue University, was appointed visiting professor of biophysics in psychiatric research at the University of Maryland School of Medicine, Baltimore.——John C. Krantz Jr., Ph.D., professor of pharmacology and head of the department at the University of Maryland School of Medicine, Baltimore, was appointed a member of the National Research Council, to represent the American Society for Pharmacology and Experimental Therapeutics in the Division of Medical Sciences. The appointment is for a three-year term.

MICHIGAN

Change in Language Requirement.—A change in the foreign language requirement for admission to the University of Michigan Medical School was approved by the regents Oct. 23. The former requirement specified a college year's study in French, German, Spanish, Latin, or Greek. The new requirement reads as follows: "Foreign Language: All applicants are required to have at least one college year of a foreign language. This requirement may be met either by completing satisfactorily a two semester language sequence in college, or by certification of equivalent achievement in a language proficiency examination." The change was requested because it is felt that an increasing number of "gifted students" will be presenting language proficiency in Russian and possibly Oriental languages.

Name Assistant Deans.—Appointment of two assistant deans for the Medical School was approved by the regents of the University of Michigan. Dr. Charles J. Tupper was appointed on a half-time basis and Dr. H. Waldo Bird Jr. was named on a three-eighths time basis, both appointments being effective Nov. 1. Dr. Tupper, director of the periodic health appraisal program for the university faculty and director of the consultation services of the University Health Service, will have responsibilities in the general administrative activities of the dean's office. Dr. Bird will continue as associate professor of psychiatry and will retain his private practice. He will be responsible for student affairs.

MINNESOTA

Foreign Speaker.—Dr. Kristian Kristiansen, professor of neurosurgery in the Ulleval Hospital, Oslo, Norway, gave a lecture, "Localized Cerebral Hypothermia and Angiography," at the Mayo Clinic, Rochester, Oct. 26.

Dr. Allen Given Heart Award.—Dr. Egar V. N. Allen, Rochester, internist of the Mayo Clinic and professor of medicine in the Mayo Foundation, Graduate School, University of Minnesota, received the Gold Heart Award of the American Heart Association Oct. 25. The award, described as "the highest honor within the gift of the association," was conferred on Dr. Allen in recognition of his "outstanding contributions in advancing the objectives and program of the American Heart Association."

Personal.—A dinner to honor Dr. John S. Lundy, Rochester, who retired from the Mayo clinic on Oct. 1, was held Oct. 10. Dr. Lundy founded the section of anesthesiology in the Mayo Clinic in 1924, at the invitation of the late Dr. William J. Mayo, and was head of that section until 1952, when he became a senior consultant.——Dr. Russell M. Wilder, emeritus member of the staff of the Mayo Clinic, Rochester, was named an honorary member of the American Dietetic Association, Aug. 27. Prior to 1959, only 10 other persons, "distinguished in fields related to nutrition," have been honored in this way.

NEW YORK

Dr. Wehrle Named Acting Microbiology Chairman.—Dr. Paul F. Wehrle, associate professor of pediatrics at the Upstate Medical Center, Syracuse, was named acting chairman of the department of microbiology by Carlyle Jacobsen, Ph.D., president of the Upstate Medical Center, and dean of the College of Medicine. The post was left open by the retirement on Oct. 1 of Dr. Orren D. Chapman, who was made professor emeritus.

Hospital News.—Dr. Martin Lazar, Poughkeepsie, was appointed director of Utica State Hospital. Assistant director of Willowbrook State School since 1950, Dr. Lazer succeeds Dr. Bascom B. Young, Utica, who retired Oct. 1.——Dr. Frederick Beck, Ray Brook, was appointed director of the State Health Department's Homer Folks Tuberculosis Hospital, Oneonta. Prior to his appointment, Dr. Beck was director of Ray Brook State Tuberculosis Hospital. He succeeds Dr. Ralph Horton, who died recently.——Dr. Lewis L. Robbins, was appointed medical director of Hillside Hospital, Sands Point. Dr. Robbins, who was secretary of the American Psychoanalytic Association, was director of the department of adult psychiatry at the Menninger Foundation, Topeka, Kan. He succeeds Dr. Joseph S. A. Miller, Glen Oaks, who retired and returned to private practice.——St. Clare's Hospital, Schenectady, held its 10th anniversary celebration during the week of Sept. 13. Sister M. Senana, SFP, is administrator of the hospital.

Hospitals Plan Merger.—The unification of the Buffalo Eye and Ear Hospital and Wettlaufer Clinic with Deaconess Hospital has the approval of the membership of Deaconess Hospital. About 100 members of the 108-member association voted in favor of the consolidation Sept. 15. Mr. Vernon A. Reed, administrator, said that under the Membership Corporation Law, the proposed unification will be submitted to the state attorney general, the State Social Welfare Department, and the State Supreme Court. The unification will be effective as soon as the three state agencies approve. The clinic and the Eye and Ear Hospital are at 52 Maple St. The first of the two institutions was founded in 1876 by the late Dr. Lucien Howe and the second in 1877. Mr. Reed said the Wettlaufer name will be continued in the enlarged hospital's operations. A current building program will increase the number of adult beds in Deaconess Hospital to 500. When the building program is completed, the present Mansperger Building will be remodeled to accomodate the Eye and Ear Bank and the clinic.

New York City

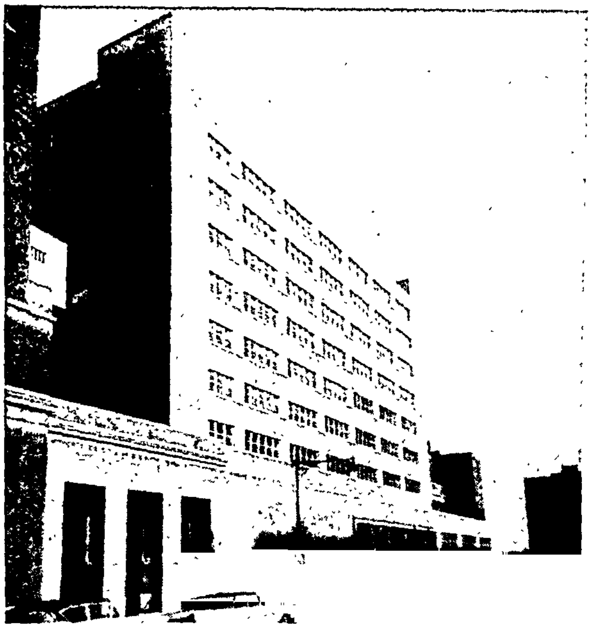
Dr. Lincoln Wins Trudeau Medal.—Dr. Edith H. Maas Lincoln, a pediatrician who pioneered in the drug treatment of tuberculosis in children, was awarded the Trudeau Medal by the National Tuberculosis Association at its annual meeting. The medal, named for Dr. Edward L. Trudeau, the first president of the NTA, is awarded annually "for the most meritorius contributions on the cause, prevention, or treatment of tuberculosis." A member of the association's board of directors since 1948, Dr. Lincoln started the chest clinic of the Children's Medical Service at Bellevue Hospital in 1922 and served as chief until her retirement in 1956.

Student Awarded Memorial Scholarship.—The Downstate Medical Center in Brooklyn awarded the second annual Dave Luckman Memorial Foundation Scholarship of $1,000 to Miss Ellen Strober, of Brooklyn. A first-year medical student at the Downstate Medical Center, Miss Strober has been a student at Smith College in Massachusetts on a full tuition scholarship. The Dave Luckman Memorial Foundation, which made possible this annual scholarship award to an "outstanding student" selected by the Downstate Medical Center faculty, was organized in 1955 by the friends and associates of Dave Luckman "to provide trust funds for the establishment of scientific educational endeavors." Mr. Luckman died in September, 1955, at the age of 35.

Personal.—Dr. Howard T. Behrman was in Rome during July and August as the official representative of the U. S. Committee of the World Medical Association to the Italian medical societies. He had several meetings and conferences with Dr. Raffaele Chiarolanza, president, National Federation of Italian Medical Societies; Dr. Carlo Prandi, president, Medical Society of Rome; and other Italian physicians.——The retirement of Dr. Arthur W. Grace, Brooklyn, from active service on the faculty of the State University of New York Downstate Medical Center in Brooklyn was announced together with his appointment as professor emeritus of dermatology and syphilology effective Sept. 1. Dr. Grace has been professor and head of dermatology and syphilology for more than 20 years.——Dr. Arthur C. DeGraff, professor of therapeutics at New York University, was named assistant medical director of *GP* magazine, published monthly by the American Academy of General Practice.

Health Department Closes Tattoo Parlors.—The City of New York Department of Health announced the closure of all tattoo parlors in the city until they are able to meet the requirements of the city's new health code. The announcement was made Oct. 1 by Jerome Tichter, assistant commissioner of the department. Previously the tattoo artists had been warned following the death from hepatitis of a 17-year-old boy in Queens General Hospital some three months after he had been tattooed in a Coney Island tattoo parlor. The announcement said that inspection of the six tattoo parlors which the Department of Health knows operate in the city showed all of them to be "in a seriously unclean and insanitary condition and lacking in suitable sanitary facilities." A new health code which went into effect Oct. 1 provides that tattoo artists must sterilize both the dyes and equipment they use and must operate in a clean and sanitary manner. The death of the 17-year-old boy was said to be the first reported in the city as due to tattooing.

Dedicate Harlem Hospital Unit.—Mayor Robert F. Wagner was principal speaker at the dedication of the new 9-story 233-bed unit of the proposed Harlem Hospital Center Oct. 5. The formal opening of the $5,500,000 facility, which has outpatient clinical services, included a tour of clinic and inpatient facilities, with Harlem Hospital nurses acting as guides. The city Board of Estimate approved the acquisition of a site on Lenox Avenue between 135th and 136th Streets, for the construction of a new 500-bed main hospital building to replace the present structure immediately to the north on Lenox Avenue from 136th to 137th Streets. Other new construction and reconstruction eventually will raise the capacity of the proposed Harlem Hospital Center to 1,200 beds, increasing present capacity by 50%. The estimated cost may exceed 35 million dollars. The new main building will include surgical and obstetrical services, a dozen operating rooms, five delivery rooms, and pathological and research laboratories.



The new 233-bed unit of Harlem Hospital Center.

NORTH CAROLINA

Annual Symposium in Chapel Hill.—The annual University of North Carolina School of Medicine Symposium will be held in Chapel Hill Nov. 24-25, with two visiting participants and 15 members of the UNC Medical School taking part. The symposium will consist of lectures, discussions, workshops, and a demonstration of an artificial kidney. The visiting participants will be Dr. Max Miller, of the Western Reserve School of Medicine, Cleveland, and Dr. Frank L. Engel, of the Duke University School of Medicine, Durham. Wives of attending physicians are invited to a coffee hour Nov. 24 and to a social hour and dinner at 6 p. m., Nov. 25. This symposium has been approved for 12 hours credit by the American Academy of General Practice.

Dr. Reeves Honored.—Dr. Robert J. Reeves, chairman of the Duke University Medical Center's radiology department in Durham was honored Oct. 16-17 at a meeting of the Reeves Radiological Society, organized by radiologists who did their residency work at Duke under Dr. Reeves' direction. Highlight of the gathering was the third Robert J. Reeves Lecture, by Dr. Charles L. Martin, professor of radiology at Southwestern Medical School of the University of Texas, Dallas, who presented "Present Concepts of Radiation Therapy of Malignancy of the Head and Neck." Dr. Reeves, a faculty member at Duke since the opening of the Medical School in 1930, was recently appointed by Gov. Luther Hodges to the North Carolina Atomic Energy Advisory Committee.

OREGON

Name Dr. Metcalfe as Heart Researcher.—Dr. James Metcalfe, of Boston, was chosen to fill the Oregon Heart Association chair of cardiovascular research at the University of Oregon Medical School, Portland. The OHA, under special arrangement with the medical school, will contribute $12,000 annually toward salary payment and will donate $7,500 a year for equipment and supplies during the first two years that the chair is occupied. This is only the second endowed chair at the medical school and the first academic chair to be endowed by a volunteer health agency in the state. Oregon is one of six states in which heart associations have set up such positions. Funds to support the chair will come from memorial contributions to OHA. The association has established a trust fund which will support the position. The chair is being established "for the purpose of enlarging the scope of research into heart and blood vessel diseases and to train young men and women in research techniques." Dr. Metcalfe, a faculty member at Harvard Medical School, will hold the academic rank of associate professor of cardiology at the UOMS. He will take up his duties in July, 1961, following a year of research and study at Tubingen University Medical School in West Germany.

PENNSYLVANIA

Appoint Professor of Hospital Administration.—Dr. Cecil G. Sheps, Boston, will join the faculty of the University of Pittsburgh Graduate School of Public Health in early 1960, as professor of medical and hospital administration. Dr. Sheps will head a program of research, field service, and advance education in the organization and administration of medical care and hospital service. Dr. John R. McGibony, who formerly headed the program, recently accepted a post as consultant to the Indian Ministry of Health for the U. S. State Department.

Hospital News.—Eagleville Sanatorium celebrated its 50th anniversary Sept. 27. Dr. Leroy E. Burney, Surgeon General, U. S. Public Health Service, and Mayor Richardson Dilworth, of Philadelphia, were among the speakers taking part. Eagleville maintains a 200-bed sanatorium for the treatment of pulmonary tuberculosis at Eagleville, in Montgomery County; and an "in-town" dispensary, social service department, and executive offices at the Jerome H. Louchheim Memorial Building, Philadelphia.

Philadelphia

Drs. Ravdin and Rhoads Named to New Posts.—Dr. Isidor S. Ravdin was elected vice-president for medical affairs at the University of Pennsylvania School of Medicine, Gaylord P. Harnwell, Ph.D., university president, announced. Dr. Harnwell also announced that Dr. Jonathan E. Rhoads, professor of surgery and former provost of the university, was elected John Rhea Barton Professor of Surgery, chairman of the department of surgery of the School of Medicine, and director of the Harrison Department of Surgical Research, posts which Dr. Ravdin had held since 1945. Dr. Ravdin, who will continue teaching in the School of Medicine as a professor of surgery, will be responsible for directing the administrative and academic activities and affairs of the University's Medical Division.

VERMONT

State Medical Election.—The new officers of the Vermont State Medical Society are: president, Dr. Frederick W. Van Buskirk, Burlington; president-elect, Dr. Benjamin F. Clark, St. Johnsbury; vice-president, Dr. Roger W. Mann, Jeffersonville; secretary, Dr. Oliver H. Durand, Bennington; treasurer, Dr. Gordon B. Smith, Rutland; auditor, Dr. Edward D. McSweeney, Burlington; speaker, Dr. John R. Hogle, Brattleboro; vice-speaker, Dr. John Van Maeck, Burlington; Delegate to A. M. A., Dr. James P. Hammond, Bennington; and Alternate to A. M. A., Dr. Gordon B. Smith, Rutland.

GENERAL

Medical Writers Award Fellowships.—The annual awarding of fellowships in the American Medical Writers' Association was made by the president of the association at the annual meeting Oct. 2. These fellowships are given "in recognition of high qualifications, personal and professional, and of established standing as a medical writer, journalist or publisher." Final approval is made by a three-fourths vote of the board of directors. Twenty active association members were awarded the fellowship certificate.

Grant Available for Study of Sterility.—The Carl G. Hartman Grant-in-Aid of the American Society for the Study of Sterility in the amount of $500 is available for 1960. Applications for this grant should be sent to the Secretary of Awards Committee of the American Society for the Study of Sterility, Dr. Robert B. Wilson, 200 First St., S. W., Rochester, Minn., by Feb. 29, 1960. No application will be considered by the committee unless it is accompanied by five copies of a brief outline of the research project for which the grant-in-aid is being sought.

Award for Paper on Decubiti.—A $1,000 cash award is offered for the "best original" 6,000-word or less paper on "Etiology of Decubitus Ulcers" by the R. D. Grant Company. The award is being made through the American Congress of Physical Medicine and Rehabilitation. The winning paper will be presented at the third International Congress of Physical Medicine, Aug. 21-26, 1960, in Washington, D. C. The contest is open to all. Judges will be the program committee for the 1960 International Congress of Physical Medicine. Complete rules are available from the R. D. Grant Company, Suite 761, Hippodrome Building, Cleveland 15.

Epilepsy Societies Form Federation.—The American Epilepsy Federation, an amalgamation of 23 lay societies in 11 states, was formed in Milwaukee Sept. 13. The purpose of the federation is "to unite all existing lay socities into a single cohesive unit." President of the federation is Mrs. Albert Grass, of Quincy, Mass. Physicians on the board of directors of the new organization are Dr. William G. Lennox, Boston, and Dr. Harriot H. Hunter, Denver, vice-presidents; Dr. Madison H. Thomas, Salt Lake City, and Dr. Augustus S. Rose, Los Angeles, directors-at-large. The federation's office is located at 77 Reservoir Rd., Quincy, Mass.

Three Physicians Appointed to Editorial Board.—The Medical Book Department of Little, Brown and Company announced the appointment of three members to its editorial board who join Dr. Chester S. Keefer, dean and professor of medicine, Boston University School of Medicine. They are Dr. Warren H. Cole, professor of surgery, University of Illinois College of Medicine, Chicago; Dr. Joseph F. Ross, professor of medicine and associate dean of the University of California School of Medicine, Los Angeles; and Dr. Irving S. Wright, professor of clinical medicine, Cornell University Medical College, New York City. Dr. Keefer will serve as chairman of the board.

International Organization of Pharmacologists.—At the 21st International Union of Physiological Sciences held in Buenos Aires in August, a Section on Pharmacology was created and empowered to arrange for symposiums, conferences, and congresses and to carry out fellowship programs as well as other activities which will contribute to the advancement of pharmacology. An organizing meeting of the new section was held Aug. 11. It was decided to build the new section around the already existing International Council of Pharmacologists, which contains one representative of each nation or region that adheres to the IUPS. The following executive committee was elected: president, Dr. Carl F. Schmidt, Philadelphia (U. S. A.); vice-president, S. Antichkov (USSR); secretary, D. Bovet (Italy); treasurer, Dr. Domingo M. Aviado, Philadelphia (U. S. A.).

Society News.—Dr. Charles A. Smith, of Norman, Okla., was elected president-elect of the **Mid-Continent Psychiatric Association,** regional affiliate society (Arkansas, Kansas, Missouri, Oklahoma) of the American Psychiatric Association. Dr. Louis A. Cohen, of Little Rock, Ark., was installed as president of the association. The other officers include Dr. William P. Kolb, of Little Rock, secretary-treasurer, and Dr. Paul S. Hines of Kansas City, Mo., editor of the Bulletin.——Mr. Lawrence J. Linck, of Chicago, was appointed executive director of the **National Association for Mental Health,** 10 Columbus Circle, New York 19. ——Officers of the **American Association for Thoracic Surgery** for 1959-1960 are: president, Dr. William E. Adams, Chicago; vice-president Dr. John H. Gibbon Jr., Philadelphia; secretary, Dr. Hiram T. Langston, Chicago; treasurer, Dr. Julian Johnson, Philadelphia; and editor, Dr. Emile F. Holman, San Francisco. The next meeting of the association will be in Miami Beach, Fla., May 11-13, 1960.

Dermatology Meeting in Chicago.—The 18th annual meeting of the American Academy of Dermatology and Syphilology will be held Dec. 5-10 at the Palmer House, Chicago, under the presidency of Dr. Anthony C. Cipollaro, New York City. Seven special courses will be conducted Dec. 5 and 6. Dr. Alexander M. Weddell, Oxford, England, will present a special lecture, "Some Observations on the Anatomy and Physiology of Common Sensation," the evening of Dec. 6. The James R. Webster Memorial Lectures will be given the morning of Dec. 7 as follows:

Corticosteroid Therapy, Dr. Cipollaro, presiding officer.
Physiology and Chemistry of the Steroids, Dr. Rachmiel Levine, Chicago.
Use and Abuse of Steroids, Dr. Francis R. Keating Jr., Rochester, Minn.

Symposiums, round-table panel discussions, clinical pathological conferences, and discussion groups are planned. Scientific and technical exhibits are arranged. The annual banquet will be held the evening of Dec. 9. For information, write the American Academy of Dermatology and Syphilology, First National Bank Building, Rochester, Minn.

Surgeons Elect Officers.—Dr. Edward L. Compere, of Chicago, was reelected president of the United States Section, International College of Surgeons. Dr. Harry E. Bacon, of Philadelphia, is the president-elect and will assume the presidency in 1960. Others elected are Dr. Arthur N. Owens, New Orleans, first vice-president; and Dr. David B. Allman, Atlantic City; Dr. Horace E. Ayers, New York City; Dr. Moses Behrend, Philadelphia; Dr. Alexander Brunschwig, New York City; Dr. Gilbert F. Douglas, Birmingham, Ala.; Dr. Earl J. Halligan, Jersey City, N. J.; Dr. Harold O. Hallstrand, South Miami, Fla.; Dr. Claude J. Hunt, Kansas City; Dr. Francis L. Lederer, Chicago; Dr. Joseph M. De Los Reyes, Los Angeles; and Dr. Gershom J. Thompson of Rochester, Minn., vice-presidents. Dr. Karl A. Meyer, Chicago, who has been secretary of the United States Section, was named honorary secretary. Drs. John B. O'Donoghue and Oscar B. Nugent, of Chicago, were named secretary and reelected treasurer, respectively.

Library on Rehabilitation.—The National Society for Crippled Children and Adults announced in its annual statistical summary report, on the Library of the Easter Seal Society, that the library contains about 3,000 bound volumes and 35,000 reprints and pamphlets covering rehabilitation and employment of the crippled and disabled. The library serves professional workers, the handicapped and their families, institutions and libraries, and health and welfare agencies. The library distributes without charge special bibliographies on cerebral palsy, employment of the physically handicapped, rehabilitation center administration, brain injury, hemiplegia, aphasia, and periodicals and books on the handicapped. For the year ending Oct. 1, 1959, 11,525 bibliographies were reproduced for distribution. The library serves as a clearing house of the society and assembles packets of literature in answer to information requests. The loan service of the library is available to professional persons. The address of the society is 2023 W. Ogden Ave., Chicago 12.

Case History Service on Oral Biology.—The American Institute of Oral Biology offers case histories from the field of oral biology for the year 1959-1960. These will include original 35 mm. Kodachrome slides of pathologic conditions of the oral cavity and jaws, accompanied by pertinent laboratory findings, medical background, roentgenograms, photomicrographs, diagnostic criteria, and whatever else may be indicated in each individual case, with a "general discussion" of the disease. A looseleaf binder and matching Kodachrome slide box will be furnished. The fiscal year of the institute is from Oct. 1 to Sept. 30. This monthly service was initiated in 1952. The subscriber to this case history service is entitled to full membership in the American Institute of Dental Medicine. Members of the A. D. A. or A. M. A. or their foreign equivalent are eligible to apply. An index of the diseases covered during this period will be mailed upon request. Complete series for the years 1954-1958 are available; the series for 1952 and 1953 are out of print. For information, address all communications to the secretary, Mrs. C. Novembri, 2240 Channing Way, Berkeley 4, Calif.

Awards for Blindness Research.—The National Council to Combat Blindness, Inc., announced 1959 Fight for Sight awards to medical colleges, hospitals, research centers and individual investigators totaling $160,000. These awards include 26 grants-in-aid, eight postdoctoral fellowships, two predoctoral fellowships, 20 summer student fellowships, and three awards in support of clinical service projects. Fight for Sight grants-in-aid and full-time research fellowships are generally awarded for a period of one year and may be renewed with the approval of the National Council to Combat Blindness' Scientific Advisory Committee. The organization announces an increase in its stipend allowance for research fellowships with a range from $2,400 to $5,000 per year to a new range of $3,600 to $7,500. Student fellowship stipends have also been increased with the maximum allowance now set at $300 per month. Student fellowships are awarded for a two- or three-month period. Jan. 1, 1960, has been designated as the closing date for receipt of applications for the 1960-1961 awards, and forms may be obtained by writing the Secretary, National Council to Combat Blindness, Inc., 41 W. 57th St., New York 19.

Anesthesiology Awards Given.—The 1959 Mead Johnson awards for graduate training in anesthesiology were granted Oct. 7, Dr. Daniel C. Moore, Seattle, president of the American Society of Anesthesiologists, announced. The scholarships, the second annual group of awards by the society to "deserving students planning careers in anesthesiology," are made possible by funds granted by Mead Johnson & Company, Evansville, Ind. Recipients of the 1959 awards are Dr. Milton H. Alper, formerly resident physician at Peter Bent Brigham Hospital, Boston; Dr. John W. Friend, a resident physician in anesthesiology at Central Main General Hospital, Lewiston, Maine; and Dr. Richard N. Winger, resident physician in anesthesiology at the University of Utah College of Medicine, Salt Lake City. The awards are made to physicians engaged in residency training for specialization in anesthesiology, and are granted on the basis of "meritorious work in clinical and research fields, and general qualifications for success in the specialty." Selection of physicians is carried out in behalf of the society by the trustees of the Anesthesia Memorial Foundation, headed by Dr. John S. Lundy, of Rochester, N. Y.

Report on Miners' Welfare Fund.—A report on the United Mine Workers of America Welfare and Retirement Fund for the year ending June 30 states that total expenditures for the fiscal year amounted to $144,151,266.51. Of this total, 97% ($139,877,814.32) were payments for 261,031 trust fund benefits, aiding 206,946 beneficiaries in all bituminous coal mining states (26). Expenditures included $78,327,652.60 for pension benefits, $57,783,116.98 for hospital and medical care benefits, and $3,767,044.74 for funeral expense benefits, widows and survivors benefits, and mine disaster benefits. About one million beneficiaries are currently covered by the trust fund for hospital and medical care benefits. Cards issued to qualified miners cover eligible dependents. Services include hospitalization, physicians' services and drugs in the hospital, specialists' services on an in-patient and out-patient basis, physical rehabilitation services, and certain drugs. Hospital and medical care expenditures during the fiscal year provided 1,343,893 days of hospitalization for 81,132 beneficiaries. Medical and surgical services for the hospitalized cases required 1,208,159 visits by physicians. Dr. Warren F. Draper, Washington, D. C., is executive medical officer of the fund.

Report on Poliomyelitis.—Paralytic poliomyelitis cases reported to the Public Health Service totaled 326 for the week ended Sept. 19, the second highest number reported for any week this year, Dr. Leroy E. Burney, Surgeon General, announced. This compares with 273 paralytic cases for the week ended Sept. 12 and 291 for the week ended Sept. 5. The highest week was Aug. 23-29, when 330 paralytic cases were reported. With the exception of the weeks ended Sept. 5 and 12, the number of paralytic cases has increased every week since May 23, when 28 cases were reported. Five states accounted for much of the latest increase. There were 26 paralytic cases in California, 26 in New York, 24 in Washington, 23 in Minnesota, and 19 in North Carolina. The Surgeon General also announced that preliminary estimates indicate there were 150 deaths from poliomyelitis as of July 31 of this year, compared with 10 by that date last year. The cases reported for the week ended Sept. 19 bring to 3,407 the total number of paralytic cases that have occurred this year. During the same period in 1958, there were 1,618 paralytic cases reported. In 1955, the first year the Salk vaccine became available, 6,864 paralytic cases had been reported by the third week in September.

Increase Budget for Pan American Programs.—Dr. Abraham Horwitz, director, Pan American Sanitary Bureau, operating arm of the Pan American Health Organization (PAHO), announced that his organization will spend $11,332,410 in carrying out 238 public health projects in the Americas during 1960. The figure represents an increase of $1,145,023 over the budget for 1959. PAHO is made up of 24 Member States, the 21 American Republics, plus France, the Netherlands, and the United Kingdom. The health organization receives its funds from four sources: (1) PAHO's regular budget, which for 1960 is 4.1 million dollars; (2) PAHO's special budget, which is made up of the Special Malaria Fund for the Americas, technical cooperation funds PAHO receives from the Organization of American States, the budget of the Institute of Nutrition of Central America and Panama, contributions from nongovernmental organizations, and donations from private foundations, governments, and citizens (the special budget for 1960 is $4,493,167); (3) the portion of the budget of the World Health Organization allotted the Bureau as WHO's Regional Offices for the Western Hemisphere, which for 1960 is $1,740,374; and (4) United Nations Technical Assistance Funds, received by PAHO through the World Health Organization, for 1960 amounting to $998,869.

Awards for Biological Research.—The Lalor Foundation announced the program of awards for 1960 which it is offering for research in the biological sciences. These awards will be for support of research on the fundamental biochemical and physiological mechanisms concerned with fertility and reproduction in various forms of life. The objectives are to further the knowledge and understanding of the basic phenomena involved and to extend and develop the possibilities for effective regulation and control. The awards may range up to $8,000 per year, depending on the scope and duration of the projects approved. Preference will be given to younger members of university and college faculty and staff with an upper age limit of 45 years. The work may be carried on at the applicant's own institution or elsewhere. The foundation will also grant postdoctorate summer or short-term research awards at the Marine Biological Laboratory at Woods Hole, Mass., or elsewhere for appropriate projects. Stipends will normally not exceed $900 for a single man or a woman, $1,000 for a married man working at his home institution, and $1,250 for a married man with a principal program at another institution. For information and application forms, write the Lalor Foundation, 4400 Lancaster Pike, Wilmington 5, Del. The final date for receipt of applications complete with supporting data is Jan. 15, 1960. Notification of appointment will be on or before March 15.

Form Agency for Schizophrenia Research.—The formation of a national voluntary health agency "to mobilize public support for research in schizophrenia" was announced Sept. 24 by its president Mrs. Godfrey S. Rockefeller. The name of the organization is RISE, Inc., for Research in Schizophrenia Endowment. RISE is a publicly supported agency whose sole purpose is to advance research into the cause, treatment and prevention, and cure of schizophrenia. The announcement was made in advance of the first joint meeting of the new organization's board of trustees and scientific council in New York City. The scientific council, which will chart the areas of research that RISE will support, is headed by Dr. David M. Rioch, director of the division of neuropsychiatry at Walter Reed Army Institute of Research, Washington, D. C. RISE has been under organization for nearly two years. During this time, it gained the assets and principal officers of the Psychiatric Research Fund when that group decided to merge with RISE. The organization also will support the training of needed personnel in schizophrenia research; stimulate the exchange of information with research groups in related fields; and conduct a public education campaign. Offices of RISE are at 9 Rockefeller Plaza, New York City.

Fellowships and Grants for Women.—The American Association of University Women Education Foundation has announced its graduate fellowships and international grants for women for the year 1960-1961. Most of the more than 35 fellowships are unrestricted as to age, field, or place of study. They may be used in the United States or abroad. The awards committee grants fellowships in general only to candidates who have received the doctorate, or who will have fulfilled all the requirements for the degree except the dissertation by the time the fellowship begins July 1. Emphasis is attached by the committee to the project on which the candidate wishes to work—its significance as a contribution to knowledge and evidence of the candidate's ability to pursue it. The candidate "must show distinction, or promise of distinction, in her field of study or research." United States citizenship is required. Requests for application forms should be accompanied by a statement of academic status. Applications, supporting material, and recommendations must reach the Committee of Fellowships Awards, 1634 Eye Street, N. W., Washington 6, D. C., not later than Dec. 1, and should be accompanied by the following: (1) a statement of advanced work and research; (2) plan for study; (3) transcripts of undergraduate and graduate work; (4) Theses, papers, or reports of investigations; a list of publications; (5) health certificate; and (6) a recent photograph.

LATIN AMERICA

Report on Mosquito Eradication.—Guatemala and Honduras declared themselves free of the *Aëdes aegypti* during the annual meeting of the Pan American Health Organization's directing council. The house-breeding *Aëdes aegypti* has been stamped out in 10 countries and three territories of the Western Hemisphere—Bolivia, Brazil, Ecuador, Nicaragua, Panama, Paraguay, Peru, Uruguay; British Honduras, French Guiana, and the Panama Canal Zone are clean of the mosquito. Programs to rid the Americas of *Aëdes aegypti* are in progress in all countries and many territories of the hemisphere, according to a report PAHO experts presented before the 24-nation council. They stated that "The Americas-wide campaign to eradicate yellow fever spreading mosquitos made considerable progress during the past year and . . . the problem is now limited to North America, and its final solution depends upon Mexico and the United States." The council, also meeting as the Regional Committee of the World Health Organization, consists of representatives of the 21 American Republics, France, the Netherlands, and the United Kingdom, PAHO's Member States.

Ophthalmology Congress in Caracas.—The sixth Pan American Congress of Ophthalmology will be held in Caracas, Venezuela, Jan. 31-Feb. 6, 1960. The tentative program, announced by Dr. Brittain F. Payne, New York City, president of the association, includes discussions on subjects ranging from genetics to autopsies, presented in symposiums, round tables, and free papers in two concurrent sessions throughout the week. Simultaneous translation of scientific papers is planned. Brig. Gen. Victor A. Byrnes, U. S. Air Force, Washington, D. C., and Dr. David E. Shoch, Chicago, will preside at the session on space ophthalmology. Speakers will consider the following subjects: hereditary conditions of the head and neck that may affect the eyes, the use of alpha chymotrypsin in the management of cataract, cataract, eye conditions that pose special problems in certain regions, strabismus, glaucoma. A series of 27 five-minute reports on progress in ophthalmic therapy will fill one morning session. Dr. Conrad Berens, New York City, will preside at a program on the prevention of blindness. Hotel and travel arrangements should be made through Dr. William L. Benedict, 15 Second St., S. W., Rochester, Minn., Chairman of the Committee on Transportation. Headquarters for the congress will be at the Hotel Tamanaco.

FOREIGN

Symposium on Drugs in Lipid Metabolism.—An international symposium will be held in Milan, Italy, June 2-4, 1960, to review the present status of biological and clinical research on "drugs affecting lipid metabolism." The agenda will include four main subjects:

(1) New data on cholesterol and lipid metabolism (biosynthesis, absorption site, catabolism, excretion, abnormal pathways).
(2) Experimental methods for the evaluation of drugs affecting cholesterol and lipid metabolism (new analytical methods and pharmacological tests).
(3) Drugs affecting cholesterol and lipid metabolism in relation to the prevention and treatment of experimental atherosclerosis.
(4) Clinical methods and therapeutical significance of drugs affecting cholesterol and lipid metabolism.

The symposium sponsored by the Institute of Pharmacology of the University of Milan, will be under the chairmanship of Prof. E. Trabucchi. Information on participation and presentation of papers can be obtained from Prof. S. Garattini, c/o Institute of Pharmacology, Via A. del Sarto 21, Milan, Italy, until March 1. The registration fee is US $10.

CORRECTION

Safety of X-ray Apparatus.—In the question and answer entitled "Safety of X-ray Apparatus," in The Journal, Oct. 3, page 630, the amount of permissible whole body exposure to gamma rays and x-rays should be "0.1 rem per week" instead of "0.3 r per week" as printed. Also, the definition given for a rad is incomplete in that a rad is not a unit for definition of beta ray energy absorption alone but is actually used more frequently to describe x-radiation and gamma radiation.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

American Board of Anesthesiology: *Written.* Various locations, June 24. Final date for filing application is January 10. *Oral.* Miami Beach, April 25-30. Applications already on file. Sec., Dr. Forrest E. Leffingwell, 217 Farmington Ave., Hartford 5, Conn.

American Board of Dermatology: *Oral.* Oklahoma City, Jan. 15-18, 1960. The final date for filing all applications was July 1, 1959. Sec., Dr. Beatrice M. Kesten, One Haven Ave., New York 32.

American Board of Internal Medicine: *Oral.* Philadelphia, March 11-12. Final date for filing application is January 15. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

American Board of Neurological Surgery: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Donald D. Matson, 300 Longwood Ave., Boston, Mass.

American Board of Obstetrics and Gynecology: *Part I, Written.* Chicago, January 16. Candidates notified of their eligibility to participate in the Part I examination must submit their case abstracts within thirty days of notification of eligibility. *Part II, Oral.* Chicago, April 11-16. Final date for filing application was August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

American Board of Ophthalmology: *Written.* January 1960 in various cities. Applications for the 1960 written examination must be filed before July 1. *Oral.* 1960, San Francisco, May; Chicago, October. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

American Board of Orthopaedic Surgery: *Part I.* Nashville, Denver and Philadelphia, Apr. 13-14. Deadline for receipt of applications is Nov. 30. Sec., Dr. Sam W. Banks, 116 South Michigan Ave., Chicago 3.

American Board of Pediatrics: *Oral.* Washington, Dec. 4-6. *Written.* Jan. 8. Final date for filing application for the written examination is Dec. 1. Exec. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

American Board of Physical Medicine and Rehabilitation: *Oral and Written.* New York, June 17-18. Sec., Dr. Earl C. Elkins, Mayo Clinic, Rochester, Minn.

American Board of Plastic Surgery: *Oral and Written.* Milwaukee, May 1960. Final date for filing application is January 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8, Mo.

American Board of Psychiatry and Neurology: New York, Dec. 14-15; San Francisco, Mar. 14-15, 1960. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 was terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

American Board of Radiology: *Examination.* Washington, Dec. 6-9. Deadline for filing application was July 1. Candidates examined in Diagnostic Roentgenology may expect to be examined in Physics. Obligatory examination in Nuclear Medicine has been postponed until after June 30, 1962 for those candidates being examined in Radiology or Therapeutic Radiology. Until that time the examination in Nuclear Medicine will be optional for those who wish to be examined in Radiology or Therapeutic Radiology. *Examination.* Cincinnati, Spring 1960. Deadline for filing applications is Jan. 1. A special examination in Nuclear Medicine (for those diplomates in Radiology or Therapeutic Radiology) will be offered provided there are sufficient applications. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

American Board of Surgery: *Written* examinations (Part I) will be held on December 2, 1959 at various centers to be announced later. Closing date for filing applications was August 1. Those completing training requirements after September 30 cannot be considered for the Part I examination in December of the same year. *Oral examinations (Part II):* Boston, Dec. 14-15; Winston-Salem, No. Car., Jan. 18-19; New York, N. Y., Feb. 15-16; New Orleans, Mar. 14-15; Kansas City, Kans., May 16-17, and Los Angeles, May 19-20. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

Board of Thoracic Surgery: *Written.* Various centers throughout the country, Feb. 12. Final date for filing application is Dec. 1. *Oral.* May 1960, Final date for filing application is Dec. 1. Sec., Dr. Wm. M. Tuttle, 1151 Taylor Ave., Detroit 2.

American Board of Urology: *Written.* Approximately 25 cities throughout the country, December 4, 1959. *Oral. Clinical* and *Examination in Pathology.* Chicago, February 1960. Final date for filing application was Sept. 1, 1959. Sec., Dr. William Niles Wishard, 30 Westwood Rd., Minneapolis 26, Minn.

DEATHS

Bankhead, Henry Miller, Eolia, Mo.; Washington University School of Medicine, St. Louis, 1930; died in the St. Louis City Hospital July 2, aged 52.

Bartmess, Leonard Ernest, Annapolis, Ill.; Chicago College of Medicine and Surgery, 1912; died Aug. 28, aged 74.

Batte, Sterling Algernon Jr. Ⓜ Gallatin, Tenn.; University of Tennessee College of Medicine, Memphis, 1952; interned at St. Joseph Hospital in Memphis, Tenn., and served a residency at the Veterans Administration Hospital in Memphis, Tenn.; veteran of World War II, receiving the Purple Heart, the Infantryman's Combat Medal, and the Bronze Star for bravery beyond the call of duty; associated with the Gallatin Community Hospital; died in the Moore–Batte Clinic Sept. 4, aged 39.

Blackledge, Theron L., Elizabethtown, Pa.; Cleveland Homeopathic Medical College, 1901; associated with the Beaver Valley General Hospital, New Brighton; died in the Harrisburg (Pa.) Hospital Aug. 17, aged 86.

Blanchard, Winthrop Eugene Ⓜ Denver; University of Colorado School of Medicine, Boulder and Denver, 1912; died Aug. 1, aged 71.

Blank, Marco Isser Ⓜ New York City; New York University Medical College, New York City, 1897; fellow of the American College of Surgeons; served on the staff of the French Hospital; died Aug. 2, aged 84.

Bowman, Galen Ford Ⓜ Toledo, Ohio; Northwestern University Medical School, Chicago, 1911; veteran of World War I; staff member of the Flower and Maumee Valley hospitals; president of the Genoa Banking Company; died Sept. 1, aged 72.

Christiansen, James Ⓜ Sioux City, Iowa; State University of Iowa College of Medicine, Iowa City, 1905; veteran of World War I; formerly county coroner; received the Silver Beaver Award for outstanding work in scouting; for many years associated with the Veterans Administration Hospital in Wood, Wis.; died in the Lutheran Hospital Aug. 28, aged 88.

Doyle, Nicholas Murray, Chicago; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1911; served with the Veterans Administration; died in the Albert Merritt Billings Hospital Sept. 8, aged 79.

Duling, Raymond Joseph Ⓜ Sioux City, Iowa; Creighton University School of Medicine, Omaha, 1929; member of the American Academy of General Practice; associated with St. Vincent's and St. Joseph Mercy hospitals, where he was president of the boards; died in Lake Okoboji Sept. 6, aged 61.

Extejt, Andrew John Ⓜ Toledo, Ohio; St. Louis University School of Medicine, 1934; interned at St. Mary's Group of Hospitals in St. Louis and the Lucas County General Hospital in Toledo, Ohio, where he served a residency at the Flower Hospital; veteran of World War II and was awarded the Bronze Star Medal; died in the Mercy Hospital July 10, aged 51.

Gehrmann, George Howard Ⓜ Chadds Ford, Pa.; born in South Norwalk, Conn., Oct. 11, 1890; Long Island College Hospital, Brooklyn, 1913; retired as director of the medical division of the E. I. Du Pont de Nemours and Company and was associate medical director until leaving the company; medical director of the Atlantic Aviation Corporation; specialist certified by the American Board of Preventive Medicine; served on the faculty of the Medical College of Virginia, Richmond; fellow of the American College of Physicians and the American Public Health Association; after his retirement, the American Academy of Occupational Medicine, of which he was a member and past-president, founded the annual George H. Gehrmann Lecture in his honor, and the Medical Society of Delaware honored him at its annual meeting for his pioneering contributions to occupational medicine and the honor he brought the society; member of the Industrial Medical Association, which in 1955 gave him the William S. Knudsen Award; formerly vice-president of the Delaware Public Health Association; at the commencement exercises on June 7, 1956, of the State University of New York College of Medicine at New York City, Brooklyn, was awarded the ninth Alumni Medallion for Distinguished Service to American Medicine; cited for his contributions to the health of workers in industry, for leadership over more than 40 years in industrial medicine, and for bringing about the collaboration of industry and medicine to protect and preserve the health of the American worker; in 1944 founded the Wilmington chapter of Alcoholics Anonymous; in 1953 a citation was presented to him by the Malvern (Pa.) Institute for Alcoholism and Psychiatric Studies, in recognition of "the exemplary leadership and courage he displayed in furthering the treatment, understanding, and welfare of the alcoholic patient and for many years of

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Ⓜ Indicates Member of the American Medical Association.

outstanding service in this cause"; a member of the President's Committee on Employment of the Physically Handicapped; veteran of World War I; served on the advisory board of the Greenbrier Clinic, White Sulphur Springs, W. Va.; since 1954 a member of the board of directors of the Memorial Hospital; died Sept. 3, aged 68.

Gober, William Mayes Jr. ⓜ Canton, Ga.; Johns Hopkins University School of Medicine, Baltimore, 1915; associated with the Kennestone Hospital in Marietta; died Sept. 4, aged 72.

Guage, Joseph Gerard, Brooklyn; Georgetown University School of Medicine, Washington, D. C., 1938; died in the Lutheran Hospital July 28, aged 48.

Hassett, Roger Gerard ⓜ Solana Beach, Calif.; University of Minnesota Medical School, Minneapolis, 1923; member of the American Academy of General Practice; formerly practiced in Mankato, Minn.; died Aug. 24, aged 63.

Hearn, James Radcliffe, Los Angeles; Georgetown University School of Medicine, Washington, D. C., 1957; veteran of the Korean War; certified by the National Board of Medical Examiners; interned at the Los Angeles County Hospital, where he served a residency; died Aug. 29, aged 31.

Heath, Samuel Horace, Denver; Central College of Physicians and Surgeons, Indianapolis, 1898; died in the Colorado State Hospital, Pueblo, Aug. 25, aged 82.

Hieber, Henry Manchester, St. Petersburg, Fla.; Western Pennsylvania Medical College, Pittsburgh, 1902; died Aug. 4, aged 79.

Hogan, Charles Vincent ⓜ Pottsville, Pa.; Hahnemann Medical College and Hospital of Philadelphia, 1919; past-president and secretary of the Schuylkill County Medical Society; served as medical examiner of the Pottsville School District; for many years a member of the board of health, of which he was president and secretary; associated with the Pottsville Hospital, where he died Sept. 2, aged 64.

Kirby, Dunne Wilson ⓜ Captain, U. S. Navy, Fresh Meadows, L. I., N. Y.; born in Philadelphia Oct. 15, 1901; Hahnemann Medical College and Hospital of Philadelphia, 1928; fellow of the American College of Physicians; in 1942 commissioned in the U. S. Naval Reserve and later in the regular Navy; served as chief of medicine at the Naval Hospital in Newport, R. I., and the Bainbridge (Md.) Naval Hospital; senior member of the physical evaluation board, Third Naval District, U. S. Navy; died in the U. S. Naval Hospital, St. Albans, Sept. 7, aged 57.

Millsap, Roy, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1903; died July 1, aged 80.

Nadler, Rose Marie Anderegg, Metairie, La.; University of Wisconsin Medical School, Madison, 1946; interned at the Philadelphia General Hospital; died in New Orleans Sept. 1, aged 37.

Passarella, Frank Anthony Jr. ⓜ St. Cloud, Minn.; Loyola University School of Medicine, Chicago, 1916; veteran of World Wars I and II; associated with the U. S. Veterans Administration; died in the Veterans Administration Hospital July 11, aged 65.

Penberthy, Grover Cleveland ⓜ Detroit; born in Houghton, Mich., March 1, 1886; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; interned at the New York City Hospital from 1910 to 1912 when he became deputy medical superintendent; served as nonresident lecturer in surgery at his alma mater; in 1913-1914 instructor in anatomy at the Detroit College of Medicine, now known as the Wayne University College of Medicine, where he was professor of clinical surgery; veteran of World War I; in 1946 awarded the Legion of Merit; according to the citation, served with distinction as service command consultant in surgery, Seventh Service Command, from July, 1942, to January, 1946; for many years chairman of the Michigan State Medical Advisory Committee to Selective Service; member of the advisory board to Surgeon General, Army of the United States, 1951-1952; in 1941 at the annual meeting of the American Medical Association, of which he was a member of the House of Delegates since 1942, and from 1938 to 1944 representative of its Scientific Exhibit, was awarded the Silver Medal with Dr. Charles N. Weller, for an exhibit illustrating the treatment of burns; past-president of the Society of Medical Consultants to Armed Forces, Wayne County Medical Society, Michigan State Medical Society, Detroit Academy of Surgery, of which he was past-secretary, Michigan Society of Mental Hygiene, Medical Veterans of World War II, American Association for the Surgery of Trauma, Central Surgical Association, American Association of Industrial Physicians and Surgeons, Detroit Academy of Medicine, of which he was past-secretary, and the Michigan Association of Industrial Physicians and Surgeons; member of the Southern Surgical Association, Western Surgical Association, American Association for the Advancement of Science, International Society of Surgeons, Association of Military Surgeons of the United States, Industrial Medical Association, Société Internationale de Chirurgie, Detroit Board of Commerce, Phi Rho Sigma, and Alpha Omega Alpha; member of the founders group of the American Board of Surgery; fellow of the American College of Surgeons, of which he was a regent and a past-governor; honorary member of the Flint (Mich.) Academy of Surgery and the Terre Haute (Ind.) Academy of Medicine; in 1954 was nominated to the Detroit Medical Hall of Fame; served as surgical director of the Michigan Mutual Liability Company; from 1950 to 1955 director and from 1954 to 1955 chairman of the board of directors of the Cranbrook School; since 1957 served on the City Plan Commission; formerly member of the Council of Social Agencies; associated with the Children's Hospital, Harper Hospital, Herman Kiefer Hospital, Receiving Hospital, Jennings Memorial Hospital, Detroit Orthopedic Clinic, Detroit Memorial Hospital, Blain Hospital, Sinai Hospital, and the Veterans Administration Hospital; died Sept. 2, aged 73.

Robinson, Gerard Briscoe, Mount Gilead, Ohio; Yale University School of Medicine, New Haven, Conn., 1924; certified by the National Board of Medical Examiners; associated with the Morrow County Hospital; died near Carey Sept. 1, aged 60.

Rupert, Margaret Jane, Cleveland; Ohio State University College of Homeopathic Medicine, Columbus, 1919; died in the Huron Road Hospital, East Cleveland, July 19, aged 67.

Salerno, John Joseph, New York City; University and Bellevue Hospital Medical College, New York City, 1910; specialist certified by the American Board of Otolaryngology; formerly on the staff of the New York Post-Graduate Medical School and Hospital; died Sept. 10, aged 72.

Shipley, Alfred Edward ® Brooklyn; Columbia University College of Physicians and Surgeons, New York City, 1899; veteran of World War I; at one time secretary of the New York City Department of Health; formerly deputy commissioner of hospitals; for many years served on the faculty of Long Island College of Medicine; member of the American Public Health Association; died Sept. 4, aged 83.

Simkus, Vincent A. ® Chicago; Loyola University School of Medicine, Chicago, 1919; died Sept. 12, aged 74.

Taran, Leo Maurice ® Great Neck, N. Y.; born July 20, 1900; Harvard Medical School, Boston, 1925; specialist certified by the American Board of Pediatrics; certified by the National Board of Medical Examiners; member of the American Academy of Pediatrics; associate clinical professor of pediatrics at the New York Medical College and Flower and Fifth Avenue Hospitals, where he was director of cardiopulmonary program; in 1955 resigned as medical and research director of St. Francis Sanatorium for Cardiac Children, Roslyn, with which he was affiliated since its founding; cardiology consultant at Meadowbrook Hospital in Hempstead and Community Hospital at Glen Cove; research consultant at Brooklyn Hebrew Home and Hospital; died Sept. 10, aged 59.

Whitby, Ferdinand Demander, Washington, D. C.; University of Illinois College of Medicine, Chicago, 1914; member of the American Psychiatric Association; served on the faculty of Howard University College of Medicine; associated with Freedmen's Hospital, where he died Sept. 4, aged 75.

White, J. Warren ® Honolulu, Hawaii; born in Roxbury, Mass., March 2, 1892; Harvard Medical School, Boston, 1917; served in the regular U. S. Navy, resigning in 1923; served as instructor of orthopedic surgery at his alma mater and at Duke University School of Medicine in Durham, N. C.; from 1938 to 1949 trustee at the Furman University, Greenville, S. C.; specialist certified by the American Board of Orthopedic Surgery, serving as a member of the board from 1948 to 1950; in 1948 went on a teaching mission to Japan and served as consulting surgeon to the Surgeon General of the Army; secretary of the Section on Orthopedic Surgery of the American Medical Association from 1944 to 1946 and chairman, 1947-1948; past-president of the American Orthopedic Association and the Western Orthopedic Association; past-vice-president of the South Carolina Medical Association; fellow of the American College of Surgeons, of which he was chairman of the Hawaii committee on trauma since 1952, and president in 1955-1956 of the local chapter; member of La Société Internationale de Chirurgie Orthopedique, American Academy of Orthopedic Surgeons, and the Association of Railroad Surgeons; consulting orthopedic surgeon to the Territorial Board of Health; chairman of the orthopedic advisory board, division for crippled children, South Carolina Board of Health for many years; chief of the orthopedic service, local base hospital unit, U. S. Public Health Service Reserve; at various times associated with the Massachusetts General Hospital in Boston, Shriners' Hospital for Crippled Children, and Greenville General Hospital in Greenville, S. C., and Oliver General Hospital in Augusta, Ga.; chief surgeon at the Shriners' Hospital for Crippled Children; member of the advisory board, and chief of fracture service, Queens Hospital; chief of fracture service, Kuakini Hospital; associated with St. Francis, Kapiolani Maternity and Gynecological, and Tripler Army hospitals; died Sept. 12, aged 67.

White, R. Rostin ® Marco, Fla.; Jefferson Medical College of Philadelphia, 1925; fellow of the International College of Surgeons and the American College of Surgeons; formerly practiced in Somers Point, N. J., where he held a post on the board of education, served as chief surgeon at Shore Memorial Hospital, and was medical inspector of the public schools; died Sept. 4, aged 58.

Wiktorin, Ervin F. K., Cleveland; Magyar Királyi Erzsébet Tudomanyegyetem Orvostudományi, Pecs, Hungary, 1934; died July 1, aged 58.

FOREIGN LETTERS

BRAZIL

Excessive Birth Weight.—The pregnancy and delivery of a macrosomic fetus is a serious obstetric problem, even for the experienced specialist. Dr. O. M. Garcia, of São Paulo (*An. brasil. ginec.* 48:65, 1959) analyzed a series of 349 babies who weighed 4,000 Gm. (8.8 lb.) or more at birth. This represented an incidence of 4.3%. The heaviest baby in this series weighed 5,790 Gm. (12.75 lb.). Overweight fetuses were more frequently born of mothers 25 or more years old, and 69.8% of the oversized babies were boys. The duration of pregnancy showed no correlation with the production of oversized babies. The fetal mortality in these babies was about three times the general fetal mortality at birth.

Mosquito Control.—The discovery of DDT led to an acceleration and expansion of the campaign against the Aedes aegypti mosquito. Dr. O. P. Severo (*Boletim de la Oficina Sanitaria Panamericana*, July, 1959) reported that the main obstacles encountered were the resistance of A. aegypti eggs to desiccation and the tendency of the mosquito in certain areas to return to its primitive habitat. Reinfestation from other countries is also a hazard. A preliminary survey was made in 1,882 of the existing 1,894 municipalities and 1,187 (63% of those surveyed) were found to be infested. A. aegypti foci were found in 244,366 of the 4,720,439 dwellings inspected. Much work remains to be done.

Strongyloidiasis.—Dr. J. M. Ferreira and co-workers of the University of São Paulo (*Hospital das Clinicas*, August, 1959) treated a series of 24 patients who had strongyloidiasis. Of these 21 were cured. Three of the 24 patients were asymptomatic. The others complained of diarrhea, abdominal tenderness, epigastric pain, meteorism, pyrosis, and nausea. The total dosage ranged between 2.1 and 12.6 Gm. given over a period of 7 to 21 days. The drug was better tolerated when it was given in small doses in the first few days of treatment. The following schedule was recommended for adults: 100 mg. in a single dose on the 1st day; 100 mg. twice on the 2nd day; 100 mg. three times on the 3rd day; and 200 mg. three times a day from the 4th to 20th day. This gave a total dosage of 10.8 Gm. Results were checked through serial stool examinations for 4 to 16 weeks after treatment. Failure of treatment in three patients was attributed in one patient to the fact that the tablets were chewed instead of swallowed, and in the other two to inadequate dosage. The treatment was successful in patients with associated whipworm and roundworm infections and was unsuccessful in one patient with associated hookworm infection. Tolerance to the drug was excellent in 10 patients. The rest complained of nausea, diarrhea, abdominal tenderness, and vomiting.

DENMARK

Is Artificial Pneumothorax Outmoded?—At a meeting of the Danish Tuberculosis Physicians' Society one speaker (*Nordisk medicin*, Aug. 13, 1959) said that, though the indications for artificial pneumothorax had gradually lessened, a few patients still require it, as when, for example, the disease is recent or subchronic, is limited to one side with small or medium-sized cavities, shows signs of relapse after what had seemed to be successful chemotherapy, or there are difficulties over alternative methods of treatment. Another speaker said that in the Silkeborg Sanatorium the numbers of patients in whom a pneumothorax had been induced in each of the six years between 1952 and 1957 were 54, 40, 33, 33, 12, and 0 respectively. In his opinion there are still patients in whom this treatment deserved consideration, although the standard routine he preferred for most patients was at least two years of continuous chemotherapy. A third speaker suggested that one reason for the growing rarity of patients requiring pneumothorax is that the group aged 15 to 34 years in which this treatment had had its greatest vogue has come to include relatively few patients.

Cancer of the Bladder.—Andersen and Glenert (*Ugeskrift for læger,* Aug. 27, 1959) reported a series of 60 patients (48 men and 12 women) who had cancer of the bladder. Their ages ranged from 28 to 87 years (mean 64). The diagnosis was verified histologically in 51 and post mortem in 4 others. Radical treatment was given to 29 and palliative treatment to 18. No treatment was attempted in 13. Among those receiving radical treatment, 21 were observed for 18 months or longer. Of these 15 achieved freedom from relapse lasting from one to more than seven years. The treatment was mainly surgical, with transurethral electrocoagulation for the smaller superficial tumors, suprapubic electrocoagulation or electroresection for larger or multiple, superficial tumors. When tumors had pene-

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The items in these letters are contributed by regular correspondents in the various foreign countries.

trated the mucosa, resection of the bladder was undertaken if possible. In recent years some improvement has been effected by combining surgical treatment with the implantation of radioactive tantalum.

Prophylactic and Palliative Treatment of Cancer.—At the Gentofte Hospital, Dr. B. Sörensen (*Ugeskrift for læger*, Aug. 13, 1959) has supplemented the operative treatment of cancer with intravenous injections of Nitromin (a derivative of nitrogen mustard) since the beginning of 1958. On July 1, 1958, he switched to Endoxan (another derivative of nitrogen mustard) which was much better tolerated than Nitromin. Nitromin was given to 48 patients and Endoxan to 29. Both were applied locally at the site of operation. While the action of Nitromin proved to be so toxic that its further administration was contraindicated, Sörensen had hopes that most patients could tolerate Endoxan. In two patients the administration of Endoxan was followed by the disappearance of metastases from anaplastic bronchogenic carcinoma. As this drug seems to be comparatively nontoxic and inflicts little discomfort on the patient, its further trial is justified.

Lithium for Manic-depressive Psychosis.—Dr. G. Belling (*Ugeskrift for læger*, July 30, 1959) used lithium to treat a series of psychotic patients (7 men and 44 women) 23 to 81 years of age with an average duration of mental illness of 48 years. Of these 32 suffered from some form of manic-depressive psychosis. Tablets containing 300 mg. of lithium carbonate were given four times a day. After a few days, the dosage was gradually reduced to a maintenance dosage of 300 to 600 mg. daily. The side-effects observed in 29 patients were so troublesome that they led to the discontinuation of this treatment in 12. The author concluded that in more than half the patients with typical mania it gave satisfactory results.

FINLAND

Suicide.—The 159 patients (55 men and 104 women) treated at two hospitals for attempts to commit suicide by an overdose of drugs are the subject of a study by Ekblom and Frisk (*Nordisk medicin*, Aug. 6, 1959). Among them were 21 whose attempt was successful at the time. Another 12 committed suicide later. The survivors were classified according to the main motives for suicide, such as matrimonial conflicts, depression connected with nervousness and insomnia, prolonged physical illness and pain, social reasons, love affairs, self-reproach, a sense of injustice, or some unknown cause.

Special attention was paid to relapses and the causes thereof, because such information might prove a useful guide to prognosis. The frequency of relapses after attempts to commit suicide because of matrimonial conflicts or love affairs was only half that of attempted suicides for the other reasons. Comparatively few relapses occurred in the group of patients inspired by a sense of injustice. On the other hand, the relapse rate was comparatively high for the victims of chronic physical illness or pain. In the last group (some unknown cause) the relapse rate was high as was the subsequent mortality. Many of the patients in this group were alcoholics and psychopaths who thus refuted the common belief that their attempts to commit suicide were demonstrative rather than serious. The authors concluded that the high relapse rate reflected adversely on the care hitherto taken in the supervision of this type of patient, and they plead for closer psychiatric control with admission to a psychiatric hospital more often than not.

FRANCE

Experimental Peptic Ulcers.—S. Bonfils and coworkers (*Archives des maladies de l'appareil digestif et des maladies de la nutrition*, May, 1959) immobilized a series of rats in latticed corselets with openings at the two ends for the four legs, which were tied to each other. The rats were horizontally suspended above the ground. Some were killed after 7 and the rest after 24 hours of constraint. Ulcers were observed in 58% after 7 hours and in 86% after 24 hours. Another series of animals was placed in cages in which five types of experimental compartments were created by mobile partitions and glass rods. The ulcers provoked by this method were the same as those induced by standard constraint. The percentage of lesions increased in proportion as the size of the compartment was diminished. There is, therefore, an inversed proportional relation between the ability to move freely and the frequency of ulcers.

Reconstruction of Blood Vessels.—At the meeting of the Academy of Surgery in March, R. Fontaine and co-workers reported a series of 323 operations for the reconstruction of blood vessels. Of 114 patients operated on for arterial obstruction 75% obtained immediate relief. In the course of the following year 50% of these arteries were again thrombosed. The site of thrombosis had an influence on the results. The best results were obtained in operations on the superficial femoral, external iliac, and popliteal arteries, in that order. The more pronounced the ischemia at the time of operation the poorer the end-result. Secondary thrombosis of a transplant did not exclude favorable clinical results; two years later and five years later such results were observed in 39 to 55%. A large percentage of secondary obliterations followed venous autografts. The authors have abandoned the use of Ivalon grafts for those of Teflon or Nylon. The technique of short circuit or of bypass gave good results in patients with spontaneous peripheral obliterations, and substitutive grafts were principally used in patients with aneurysm.

ISRAEL

Rheumatic Fever.—At a meeting of the Israel Medical Association, A. Brand-Auraban of Jerusalem stated that the mortality from rheumatic heart disease in Israel is between 10 and 13 per 100,000. In childhood the mortality is greater than for all of the infectious children's diseases combined. The death rate increases with age, being 3 per 100,000 in the group 0 to 4 years of age; 12 per 100,000 in the group 45 to 64 years of age; and 53 per 100,000 in the group aged 65 and over. In about 20% of the fatal cases, the rheumatic fever was incurred before 24 and in 50% before 44 years of age. In Jerusalem the death rate from this cause is about 60% higher than in the country as a whole.

The annual incidence of acute rheumatic fever in Israel is about 1.5 per 1,000 population while in Jerusalem it reaches 6.5 per 1,000. Yearly 2,500 to 3,000 cases of rheumatic fever are reported in Israel; 70% of the patients have their first attack between the ages of 5 and 15 years and 40% between 5 and 9 years. No parallel exists between the incidence of streptococcic diseases, such as scarlet fever or acute tonsillitis, and rheumatic fever. The meteorological factors of the Jerusalem climate are taken into consideration, especially the dryness of the air and the difference between day and night temperatures, to explain the higher incidence of rheumatic fever. No definite seasonal pattern was found for the incidence of acute rheumatic heart disease.

Outbreak of ECHO Virus Infection.—At the same meeting, L. Rannon and co-workers reported on an outbreak of aseptic meningitis. The 22 patients with meningitis and 13 abortive cases were concentrated chiefly among children 4 to 10 years of age. Few cases occurred in infants and adults. The disease was characterized by fever of 2 to 10 days' duration (in some patients biphasic), headache, vomiting, somnolence, and signs of meningeal irritation. Most patients showed a tendency to hyperreflexia. Among those with meningitis two developed flaccid paresis of the lower limbs, and one of them still had some weakness in his legs on follow-up examination three months after onset. Attempts were made to isolate viruses from stools and throat swabs. Twelve monkey kidney cell cytopathogenic agents were isolated from eight patients and one contact. All strains proved to be immunologically related or identical with ECHO virus type 9. Tissue culture neutralization tests for ECHO virus 9 antibody were made on blood samples taken during the acute and convalescent phase of the disease. In many patients fourfold or higher rises in antibody titer were observed. In 87% of those with meningitis and 85% of the abortive cases ECHO virus 9 infection was proved. Most of the control patients showed no ECHO virus antibodies.

NETHERLANDS

Salmonellosis.—According to F. Dekking (*Parool*, Aug. 22, 1959) until a few years ago only about 20 members of the genus Salmonella could be found in the Netherlands. Since then, however, this number has increased with about 10 new types being identified yearly. Some of these new specimens have previously never been found anywhere else in the world. Others are brought in with all sorts of cattle fodder, which contain fish meal and other animal foods from Africa, South America, and Asia. Several months after their arrival they can be found in slaughter cattle and later they appear in the human population.

A Fifth Type of Phakomatosis.—E. H. Hermans and co-workers (*Nederlands Tijdschrift voor Geneeskunde*, 1959) observed a boy who at 3 years of age began to develop many small tumors on his skin. At first these tumors were mainly located on his neck and shoulders, but later were found on other parts of the body. When the boy was 13 years of age the number of these tumors was still increasing. Initially these tumors looked like small fibromas, but later they became more elevated and pedunculated. They grew darker and finally looked like verrucoid nevi. Microscopic sections showed the growths to be benign epitheliomas. The authors suggested the name nevus epitheliomatosa multiplex. According to the authors, these lesions have never been described before. Shortly after his birth one of the patient's eyes was removed for fear it might contain a retinal blastoma. A further examination of the enucleated eye led to the diagnosis of dysgenesis oculoneuroblastica gliomatosa. The electroencephalogram revealed some abnormalities. These findings, in general, resembled a group of diseases which in 1932 was called the phakomatoses and which includes multiple neurofibromatosis, Hippel-Landau's disease, nevoid amentia, and adenoma sebaceum. All of these disorders present nevus-like changes of the skin, ocular abnormalities, and changes of the central nervous system.

The Paul-Bunnell Test.—L. C. Klijn (*Nederlands Tijdschrift voor Geneeskunde*, 1959) stated that the Paul-Bunnell test as originally performed with unprepared serum was not sufficiently reliable to establish the diagnosis of infectious mononucleosis. Apart from several other conditions in which a positive test might be encountered, the test could be negative in a patient with an obvious case of infectious mononucleosis. This unreliability was caused by the fact the human serum might contain three different types of agglutinins, all of which agglutinated the red blood cells of sheep. These included the Frossman agglutinins, which might be encountered in healthy persons, the serum sickness agglutinins, and the agglutinins of infectious mononucleosis. In 1937 Davidsohn proposed to first subject the serum to be investigated to an absorption by a suspension of guinea pig kidney cells, by which method the Frossman and the serum sickness agglutinins are removed from the serum.

The present author investigated the reliability of this indirect Paul-Bunnell test. A series of 4,255 samples of serum of healthy subjects and of patients suffering from other diseases gave a titer of 1:8 or 1:16 in only seven instances. These seven positive tests included only abnormalities, which were in no way related to infectious mononucleosis. Furthermore, in all of the 25 patients with an obvious infectious mononucleosis a positive result was obtained. When a serum was investigated on several occasions or with the cells of different sheep, no large variations in the titer were observed. Such variations were common when the original technique was followed. Finally the author pointed out that a microscopic indirect test could be done on a slide. In this way the result could be obtained within one hour. If the slide test is negative a macroscopic control test with test tubes is necessary.

NORWAY

Cancer Registration.—As early as 1907 the first national cancer registration was started by the Cancer Committee of the Norwegian Medical Association in conjunction with the Norwegian Public Health Service, but such registration did not become effective till 1952 when cancer and allied conditions were included among the compulsorily reportable diseases. By the end of 1956 sufficiently reliable information had been collected to warrant the publication of the observations of the Cancer Registry in the two-year period 1953-1954. (Cancer Registration in Norway, The Incidence of Cancer in Norway 1953-1954). Its authors are Einar Pedersen and Knut Magnus. The publication of this report in English puts it at the service of many foreign research workers interested in the progress made in this field in Norway. In the two-year period reviewed, 7,684 new male and 8,044 new female patients were reported. The part played by sex in the incidence of cancer in different sites comes out plainly in connection with the lips. Thus, the incidence of cancer of the upper lip was nearly the same for the two sexes, but there were 25 male to 1 female patient with cancer of the lower lip. The lip was one of the few sites showing, among men, generally higher morbidity in rural than in urban areas.

Biopsies of Lymph Nodes.—At Professor Kreyberg's University Institute for General and Experimental Pathology an opinion has often been given on enlarged lymph nodes removed from apparently healthy persons with a normal sedimentation rate and blood count. Dr. O. H. Iversen (*Tidsskrift for den Norske Laegeforening*, Aug. 1, 1959) reported a 3-to-12 year follow-up. Of these, 42 were apparently healthy and had malignant lymphoid disease but were still living. The author cautioned against *a too facile diagnosis of malignant disease*, because great misery is thus inflicted on the patient whether it is correct or not. Even if it is so, little can be gained by the knowledge, since the enlarged gland may merely be the outward expression of a deep-seated systemic disease refractory to a radical cure by the surgical, radiologic, chemical, or hormonal treatments available. This is so however intense the regional treatment may be. It is therefore well to give the patient the benefit of the doubt when the diagnosis is in question and to diagnose a benign condition even at the risk of subsequently being proved wrong in some cases.

Poliomyelitis Vaccination.—The experiences with poliomyelitis vaccination since it was started were reviewed by Dr. F. Mellbye (*Tidsskrift for den Norske Laegeforening*, Supp. 16, 1959). The author stated that late in 1956 about 500,000 persons were given two injections of the vaccine, but the comparative freedom from poliomyelitis enjoyed by Norway in the following year prevented evaluation of the efficacy of this measure. The chance to do so came with the epidemic of 1958 when 236 paralytic patients came under close observation. In 232 of these patients accurate data were available. The following conclusions were drawn. There was no evidence to show that the vaccination had provoked a single case of poliomyelitis. Complications of vaccination were rare. Among children vaccinated twice and thrice, the frequency of new paralytic cases was only about 20% of that for unvaccinated and once-vaccinated children. The author was unable to determine whether paralysis in vaccinated persons had been less severe than in the unvaccinated.

SWEDEN

When Legal Abortion Is Refused.—To determine what happens to the women who apply to the authorities for the induction of abortion and are refused Dr. G. Hultgren (*Nordisk medicin*, Aug. 6, 1959) examined the records of 4,274 persons. They were classified according to geographical distribution, age, marital status, and other conditions. About 86% allowed their pregnancies to go to term. The rest aborted spontaneously or in response to criminal methods in a proportion impossible to assess accurately. Obstetricians commonly agree that at least 10% of such pregnancies end in spontaneous abortion. In Stockholm this figure was found to be 15.7% and for other parts of Sweden about 13.6%. Among all the women in this series only one committed suicide. This refutes the common theory that women who have been refused induction of abortion will commit suicide.

Delirium Tremens.—A series of 240 patients at the Beckomberga mental hospital were treated for delirium tremens and allied conditions with Hemineurine by Dr. E. Giacobini and co-workers (*Nordisk medicin*, Aug. 6, 1959). Some were given the drug by mouth, some by intravenous injection, and others by both routes. A single intravenous injection induced deep short-lasting sleep. There were no serious complications and the results were encouraging. In the same issue, Dr. E. Osterman and co-workers reported a series of 28 patients who had manic psychosis, anxiety states, status epilepticus, and schizophrenia whom they treated with the same drug. Their results were also encouraging, though not as good as those of the French workers who introduced the drug. Hypotension and digestive disturbances were commonly observed side-effects when the drug was given by mouth.

Treatment of Smoking Addicts.—In *Svenska Läkartidningen* (Aug. 14, 1959) Dr. B. Ejrup traced the smoking habits of 1,012 patients after they had undergone his system of treatment which consisted of a 10-days' course of subcutaneous injections of lobelin hydrochloride supplemented by meprobamate and Secergan tablets. The immediate results were good, 75.6% having been weaned of their cigarette smoking. These patients had previously tried in vain to effect a cure by themselves. The subsequent habits of 903 were followed and the relapse rate was found to be lowest among the smokers who had promptly ceased to smoke after only a day's treatment. After six months 76% in this category had not relapsed. The risk of relapse dwindled with every month of abstention.

UNITED KINGDOM

Mothers Sent Home Twenty-four Hours After Births.—Mothers should be sent home from the hospital 24 to 28 hours after a normal delivery according to Dr. G. F. Abercrombie (*Lancet*, Sept. 19, 1959). This not only would relieve the shortage of hospital beds but also would prove a real advantage for mother and child. In 1951 emergency applications for maternity beds varied from 150 to 300 a quarter but are now 800. The reason is the failure or inability of antenatal clinics to make a reservation in advance. As a result the baby is often born in unsuitable conditions at home before there has been time to find a hospital bed, or in the ambulance on the way to the hospital. It is fairly generally accepted that, provided home conditions are acceptable, and domestic help is available, mothers can go home soon after giving birth. One stumbling block is over the training of midwives, and the sharp division between hospital and domiciliary midwives. Sending mothers home early means that the midwife who attended the birth would not see the case through the 14-day puerperal period, which has been thought desirable.

International Social Security.—A social security agreement between the United Kingdom and Denmark, covering all benefits under national insurance, industrial injuries insurance, and family allowances schemes in both countries, has been signed and will be effective when ratified. Contributions paid in both countries may be added together to qualify for benefit. In addition, British nationals and their dependents will be able to get urgent medical treatment under the Danish sickness insurance scheme, whether they are working in Denmark or on holiday there.

Armed Forces Medical Services.—An annotation in the *British Medical Journal* of Sept. 5 stated that the fourth report from the Select Committee on Estimates recommended integration of the medical services of the armed forces. The committee believed that this would save money and manpower and increase efficiency. A joint service would have the advantages of greater size and scope and medical officers in it would gain wider clinical experience. To these advantages the committee added those of greater flexibility in the deployment of specialists and of the need for a smaller administrative staff, which would reduce expenditure and release a number of senior medical officers for professional duties.

Integration of the medical services of the armed forces has been considered at intervals since 1946. The Forces Medical and Dental Committee thought amalgamation undesirable, as also did the BMA in presenting its evidence to that committee, because of the specialized needs of each service, their differing tasks and functions, and hence their different organizations and the need to preserve the *esprit de corps* engendered by loyalty to an individual service. The Select Committee, however, believed that the size and function of the services had altered so much that the forces committee's views were to some extent invalidated. The BMA did not think so, and repeated its objections to integration in its evidence to the Select Committee; the service departments' attitude to it is described by the Select Committee itself as being disappointingly inflexible.

CORRESPONDENCE

TREATMENT OF ULCERATIVE COLITIS

To the Editor:—With reference to the article entitled "New Treatment for Ulcerative Colitis" by Louis W. Granirer, which appeared in The Journal, Sept. 26, page 402, it would be most unfortunate if the writer would infer that ulcerative colitis should be treated by administration of gold salts and phenylbutazone and an unrestricted diet of roughage, fried and fatty foods, and pizza pie. I assume that such was not the author's intention. As a physician who has been duly battle-scarred through numerous encounters with chronic, acute, and fulminating cases of ulcerative colitis, I strenuously caution the general practitioner against making use of such short cuts to success.

The author has reported the case of a critically ill patient who was dehydrated and in nutritional failure. By his own admission, "saline solution and blood were infused at a rapid rate." Antibiotics, corticosteroids, ACTH (intravenously), and vitamin B_{12} (subcutaneously) were also given. This therapy alone was adequate for the patient's dramatic recovery. The administration of gold salts twice weekly and 100 mg. of phenylbutazone daily by mouth cannot be construed as the "new treatment" that turned the clinical course. These compounds were once used in the management of rheumatoid arthritis, a distressing complication of ulcerative colitis. They have been replaced by ACTH and the adrenal steroids. The use of gold salts in a patient seriously ill with colitis may add fuel to the fire. Although the author was careful to use only 5 mg. of gold sodium thiosulfate, in the occasional sensitive patient this dose would be sufficient to cause severe toxic manifestations such as pruritis, gastroenteritis, stomatitis, exfoliative dermatitis, or thrombocytopenic purpura, or any combination of these. Phenylbutazone has been known to cause a fatal depression of the marrow. Finally, a physician with any experience in this field should know that fatty and fried foods, raw fruits and vegetables, nuts, and pizza pie stimulate peristalsis. Therefore, the title of the article, "New Treatment for Ulcerative Colitis," is misleading and disappointing because it suggests new therapy, which is not, in reality, what was given.

William Z. Fradkin, M.D.
27 Prospect Park West
Brooklyn 15, N. Y.

To the Editor:—The article, "New Treatment for Ulcerative Colitis," by Louis W. Granirer in The Journal, Sept. 26, page 110, is of interest to us because of our experience with phenylbutazone in treating patients with this disease. Our negative results, obtained early in 1958, acquire pertinence in view of Dr. Granirer's report. We treated six patients with ulcerative colitis during acute exacerbations of moderate severity but without complications. In two patients the onset was recent; they had received no previous treatment. Phenylbutazone was the sole drug given, moderate dietary limitation being the only other therapy (except in one patient who had been receiving small doses of prednisone and antispasmodics, without relief, and who continued to take these drugs). The dosage of phenylbutazone was 300 to 600 mg. daily for one week. The response was evaluated by the proctoscopic appearance before and after treatment as well as by symptoms. Only two of the six patients showed symptomatic improvement. One of these was the only patient in the series to show definite improvement proctoscopically. A toxic reaction, consisting of a skin rash, was encountered in one patient. The results obtained were, we believe, in accord with the naturally variable course of untreated ulcerative colitis and failed to indicate any effect from phenylbutazone.

We do not claim that these negative results necessarily disprove any possible usefulness of treatment with phenylbutazone in patients with ulcerative colitis, but experience with proved therapy such as steroids would suggest that if phenylbutazone had any comparable degree of efficacy it should have been manifest under the circumstances of our study. Although the dosage given to our patients was much higher than that of Dr. Granirer's, in both his case report recently published in The Journal and his previously published report (*New York J. Med.* 58:3467 [Nov. 1] 1958), he used the drug for longer periods and in conjunction with a gold salt. His earlier article does not include any individual description of the patients treated nor the details of the basis for evaluating their response.

In interpreting the result in the case reported in The Journal, several cautions are necessary. Although an acute fulminating exacerbation of ulcerative colitis is a serious condition, Dr. Granirer properly points out in his opening paragraph that about 64% of such patients recover, at least temporarily, from the acute episode. In these the severe toxic manifestations may pass almost as quickly as they come on. The course is so variable that no general conclusion can be drawn from a single case. ACTH, in doses that need not be large, is particularly effective in promoting rapid remission, and correction of fluid and electrolyte depletion is also an important measure tending to cause improvement. Dr. Granirer's patient received blood and fluids intravenously, corticosteroids in unstated doses, antibiotics, and significant amounts of ACTH —in addition to the "new treatment"—and clinical improvement clearly occurred in temporal relation to the former measures rather than to the latter. The eventual degree of recovery, with residual involvement of the left half of the colon shown on barium enema, is no greater than we have witnessed in patients who were given only supportive therapy, and who might represent the natural process of healing. In short, the report left us with much doubt that it was the "new therapy" that saved the colon and the life of the patient.

As we face this disease, whose cause is imperfectly understood, armed with drugs whose mechanism of action (if any) is largely unknown, we are justified in being empirical; but, in the case of drugs having as much potential toxicity as phenylbutazone and gold, caution must temper empiricism. Most important of all, such empirical attempts will be productive only if critically evaluated.

Lee M. Hershenson, M.D.
Morris A. Hershenson, M.D.
3700 Fifth Ave.
Pittsburgh 13.

EMERGENCY CARE OF EXTRADURAL HEMATOMA

To the Editor:—In The Journal, Sept. 26, page 405, in the article "Emergency Care of Extradural Hematoma," Drs. Craig and Hunt describe a procedure which they recommend for the general surgeon who may have to treat this surgical emergency in the absence of neurosurgical help. After the temporal fossa has been opened and the clot evacuated, bleeding may not be controllable except by packing the foramen spinosum. This maneuver may not be possible for the surgeon untrained in neurosurgery, but the general surgeon can readily find and ligate the external carotid artery in the neck, which serves the same purpose.

Paul R. Rosenbluth, M.D.
104 S. Michigan Ave.
Chicago 3.

SPONTANEOUS REGRESSION OF MALIGNANT TUMORS

To the Editor:—In a letter in The Journal, Aug. 8, page 1842, Dr. Edward Bierman suggested that lysozyme may be a chief factor in the spontaneous regression of malignant tumors. This statement of extreme oversimplification should be challenged. The cause of spontaneous regression is still unknown. Careful study of each reported case of spontaneous regression (Pelner: *J. Am. Geriatrics Soc.* 4:1126 [Nov.] 1956) has failed to show any possible connection between the enzyme, lysozyme, and spontaneous regression. Many substances are carcinostatic and even carcinolytic in lower animals, but the results do not carry over to human beings.

Concerning lysozyme metabolism in man, Meyer and co-workers (*Proc. Soc. Exper. Biol. and Med.* 65:220 [June] 1947, and *Am. J. Med.* 5:482 [Oct.] 1948) assayed the lysozyme content of stool specimens from various groups of patients, and the results showed a 27-fold increase in the mean titer of stools of patients with chronic ulcerative colitis over that of stools from normal persons and a 46-fold increase over that of normal persons after purging. The colonic mucosa of patients with acute ulcerative colitis showed an 8.5-fold increase in lysozyme content over that of colonic tissue in normal persons. The mean output of lysozyme in the stools of patients with chronic ulcerative colitis over a 24-hour period was 168 times that in normal stools.

Let us examine the incidence of carcinoma of the colon in patients with chronic ulcerative colitis, the very persons supposedly protected by a high lysozyme content of their mucosa. The weight of expert opinion is that ulcerative colitis predisposes the patient to the development of carcinoma of the colon. Cattell (*Gastroenterology* 10:63 [Jan.] 1948) reported colonic tumors in 7% of all patients with ulcerative colitis who came to surgery; in those who had the disease for nine or more years, 33% developed carcinoma. Kasich and co-workers (*N. Clin. North America* 33:142 [Sept.] 1949) reported an incidence of 4.9%. Ferguson and Stevens (*Gastroenterology* 11:640 [March] 1948) emphasized the danger of delaying colectomy in patients with longstanding ulcerative colitis lest a rapidly mestastasizing colonic carcinoma develop. Colcock (*New England J. Med.* 242:320 [March 2] 1950) stated that in patients with ulcerative colitis of a duration of more than eight years, the incidence of carcinoma was 30%. Mackie reported that 7% of his pathological material from patients with ulcerative colitis showed carcinoma, while Cave reported an incidence of 8%, and Brandes found 4.25% (Lyons and Garlock: *Gastroenterology* 18:170 [June] 1951). The lowest figure reported in the symposium is three or four times the incidence of carcinoma found in the general population.

While it is true that carcinoma of the lens is exceedingly rare, this may be due to special circumstances rather than carcinostatic substances in the lens. The immunological properties of the lens protein have been extensively investigated (Bourne: *Physiol. Rev.* 17:1 [Jan.] 1937). Unlike other tissue proteins, they are organ-specific and species-nonspecific. This means that their chemical structure is the same in all species and that they differ from the general tissue proteins so markedly that they are capable of acting as foreign proteins. When lens extracts are injected into an animal, precipitins and complement-fixing antibodies appear in the blood, and these react in the test tube with lens extracts from all vertebrate species. Perhaps, normally, the growth pattern of the lens is controlled by the antibody present, which would prevent an exaggerated rate of growth. The immunological properties of lens proteins must be considered carefully before it is planned to inject them in human beings.

Dr. Louis Pelner
1352 Carroll St.
Brooklyn 13, N. Y.

CARDIAC ARREST

To the Editor:—The author of "Successful Treatment by a Chest Blow of Cardiac Arrest During Myocardial Infarction" in The Journal, July 11, protein have been extensively investigated. page 1307, is to be complimented on his prompt recognition and treatment of cardiac arrest. However, the history of sudden severe pain deep in the midsternal area, with radiation to both arms, normal respiratory rate and temperature, increasing pain despite opiates, and maintenance of blood pressure of 150/80 mm. Hg, suggests a dissecting aneurysm. This view is strengthened by the author's report of the five normal and static serial electrocardiograms made over a seven-month period and four normal transaminase test results. In this case the dissection must have healed spontaneously, as it frequently does, but there is a tendency to recurrence because of the presence and progression of the underlying aortic disease. Under these circumstances, it would be inadvisable to institute a long-term program of anticoagulant therapy, which might aggravate a future dissection.

Nathaniel E. Reich, M.D.
135 Eastern Pkwy.
Brooklyn 38, N. Y.

EPIDEMIOLOGY OF THE FUTURE

To the Editor:—I have read the editorial in the Sept. 12 issue of The Journal, page 188, on "Epidemiology of the Future," as well as the article by Milton Golin to which it referred. I consider it imperative that every general practitioner and specialist read both. You are correct in pointing to the great advance in the recognition of mental illness as a disease entity. More significant, from the general physician's point of view, is the factor of externally imposed emotional disturbance in the whole spectrum of somatic diseases.

From the standpoint of my own specialty, which is the cardiovascular system, my experience over three decades convinces me that no less than 70% of cardiovascular disease is caused by environmental stress. We may not be able to change society, but we may, at least, observe gradual modifications for the better that take place in an evolutionary way from generation to generation.

What we can do is to recognize the terrific, deleterious impacts that stem from difficulties in family adjustments, for example—difficulties within, which conflict with forces from without, to prevent healthy family integration. The struggle to keep up with the Joneses—the conflict between love and lovers, as depicted in the movies and on television on the one hand, and the reality in the home, on the other—these, and other external motivations symbolized by the big, shiny car and the plethora of expensive paraphernalia—these things and their difficulty of attainment tend to produce stresses which damage the circulatory system. Examples in our offices daily make it evident that the trouble lies not solely in the individual person but in the conflicting values imposed on him or her by our status-seeking society. For too many, the artificially generated urge is too great to bear with equanimity. These are some of the causative factors of the type of disorder referred to in "Epidemiology of the Future."

Joseph B. Wolffe, M.D.
Valley Forge Heart Hospital
and Medical Center
Norristown, Pa.

COLOR BLINDNESS AND HUNTING

To the Editor:—It has occurred to me that a few lives can be spared during the hunting season, and perhaps on the highway, in consideration of the fact that 4% of men and 0.5% of women are color blind. In Minnesota there are from three to eight accidental hunting deaths every year. Minnesota sold about 225,000 hunting licenses in 1958. This would mean about 10,000 color-blind persons in the woods hunting deer. Blue-yellow blindness is rare. Almost all color-blind persons have protanopia—red blindness—and deuteranopia—green blindness. Since almost all states have rulings requiring deer hunters to wear red clothing, a few of the accidental deaths must be due entirely to color blindness. In a totally color-blind person all colors vary in their degree of brightness from white through grays to black. Persons with red-green blindness are often unaware of this fact and resent being informed of it.

Visual examinations are made by the highway departments of all states, but color blindness, I believe, is not tested for. If it is I have never heard of a person being denied a license on the strength of it. In those states where there is no color-blindness examination, it would take only a few minutes to test for blindness for the major colors, with use of the American Optical Companies' pseudoisochromatic plates for testing color perception. I believe these tests would save many lives in all states.

Hubert Waldemar Lee, M.D.
614½ Laurel St.
Brainerd, Minn.

MISCELLANY

FACTS ABOUT DRUGS AND DEVICES FOR WEIGHT REDUCING

According to a news release dated September, 1959, from the Food and Drug Administration, the following information about types of products currently or recently marketed for weight reducing represents the consensus of informed medical opinion about the usefulness, limitations, and hazards of use, if any, of these products.

Electric vibrator devices include hand units, pillows, chairs, tables, and even mattresses. All furnish vibration by means of an electric motor with a rotating mechanism off-center from the drive shaft. Some also contain a heating element. Some people enjoy the sensation provided by the vibration of some of the devices. This vibration may, in some cases, provide temporary relief for minor muscular aches and pains due to fatigue or overexertion. Vibration has no other therapeutic effect, although false claims have been made that these devices will prevent or cure many serious diseases. No device is effective for "spot reducing," "melting away fat," or "breaking up fatty deposits." Vibration or other massaging devices should not be applied to inflamed areas and would be dangerous if applied to legs or thighs in patients with thrombophlebitis.

Girdles and garments have no value in weight reduction, although they may have the effect of redistributing the bulges to make them less noticeable.

It does not make sense to overeat and then try to offset the effects by taking purgatives or laxatives to rush the food through the body before it can be absorbed. Frequent or continued use of laxatives produces chronic irritation of the gastrointestinal tract, and if laxatives are taken in sufficiently large amounts for a sufficient period to be effective in weight reduction, the balance in the absorption of nutritional factors will be upset. Bulk laxatives have been sold with claims that they fill the stomach and thus depress the appetite, but since such products do not produce bulk in the stomach (they work only in the intestine), they are not effective in cutting down the appetite or in reducing.

Any drug which would stimulate metabolism to such an extent that it would cause weight loss is much too dangerous for use without medical supervision. Conversely, any drug which is safe enough to be bought without a prescription will have no value for weight reducing based on its effect on the body metabolism.

Several of the popular appetite-depressant drugs sold without a prescription contain phenylpropanolamine as the active ingredient. This drug produces no useful appetite-depressing effect. In small doses the net effect in reducing weight is negligible. In doses large enough to produce a significant effect in reducing weight (available only on prescription in any event), the undesirable side-effects nullify its usefulness. The active ingredient of a chewing gum sold as an appetite depressant is benzocaine. This is supposed to anesthetize the taste buds or the hunger mechanism of the stomach, but this effect has not been verified. There are certain drugs, safe only for use on a doctor's prescription, which will depress the appetite temporarily. These are of real value in a properly designed dietary program while a person is being reeducated in his eating habits, but their effects gradually wear off unless the dosage is progressively increased. When the drug therapy is discontinued, the appetite may suddenly return to normal or even greater than normal. Thus, any weight lost will be promptly regained unless the reeducation process has been successful in enabling the patient to control food intake by sheer will power.

There are drugs which will cause a temporary loss of water and a corresponding weight reduction, but this is not a reduction in the amount of body fat, and the weight loss is therefore an illusion without real significance. Many of the products so marketed contain a recommendation for dosages which may actually cause weight gain rather than weight loss.

There is no vitamin, mineral, protein, or other food supplement that will produce a reduction in body weight. Protein has roughly half the caloric value of fats, and to the extent that protein can be substituted for fat in the diet, the diet will be less fattening. People on an extremely restricted diet, limiting the variety of food eaten, may need vitamin or mineral supplements to maintain good nutrition, but even a moderately severe diet, such as would normally be prescribed for weight reduction, does not require a vitamin-mineral supplement if it is properly chosen. In any event, supplementary vitamins and minerals would not help directly in losing weight. Some of the promotional schemes for such supplements have suggested, at least indirectly, that the product will automatically reduce weight without any change in eating habits. Careful reading of the entire plan, however, reveals that a low-calorie diet must be followed to produce results.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

Spontaneous Pneumothorax in Apparently Healthy Flying Personnel. G. Dermksian and L. E. Lamb. Ann. Int. Med. 51:39-51 (July) 1959 [Lancaster, Pa.].

Twenty-five persons who had experienced 38 episodes of spontaneous pneumothorax were studied at the School of Aviation Medicine, having been referred after the involved lung had reexpanded. The study included a detailed history, a physical examination, blood count, hematocrit, erythrocyte sedimentation rate, fasting blood sugar, urinalysis, and electrocardiogram. In addition, pulmonary function tests and a variety of roentgenographic techniques, including routine posteroanterior and lateral chest x-rays, apical lordotic views, and apical laminagrams, were made. In 11 of the cases, additional anteroposterior films were taken in the altitude chamber at simulated altitudes of 10,000, 20,000, 30,000, 40,000, and 43,000 ft. with pressure breathing. Three of the 25 persons had a total of 11 pneumothoraces in an aircraft or in the altitude chamber. In one of these persons the first 2 episodes occurred in flight, and the subsequent 4 episodes occurred in the altitude chamber during diagnostic studies. Spontaneous pneumothorax occurring in aerial flight was disabling because of the pain, the dyspnea resulting from the altered ventilatory function of the lung, and the already existing problem of hypoxia at altitude. After reexpansion of the involved lung, pulmonary function tests of ventilation were within normal limits in all 25 cases. The routine posteroanterior and lateral chest x-rays disclosed pathological entities (cysts, emphysematous bullae, or pleural blebs), which would account for the spontaneous pneumothorax in 7 of the cases. In an additional 7 cases apical laminagraphy revealed the pathological etiology.

There are 4 pathological entities which must be considered as etiological factors of spontaneous pneumothorax: (1) pleural adhesions; (2) congenital cysts of the lung; (3) scar tissue vesicles; and (4) emphysematous valve vesicles. It is suggested that these entities are usually bilateral in occurrence. The impression that congenital cysts, scar tissue vesicles, and emphysematous valve vesicles are entrapped-air sacs was given further credence by x-ray studies in the altitude chamber. It is interesting that the initial symptoms were not severely incapacitating in the 22 patients in whom the pneumothorax occurred at ground level, but each of the episodes which occurred during aerial flight in the 3 remaining cases was of sufficient severity to incapacitate the individual.

The therapy of small, benign, uncomplicated spontaneous pneumothorax is primarily bed rest. In this series of 25 cases, therapy was carried out by different physicians and reflects differences in their training. Five patients required no treatment of any kind; 13 required bed rest of less than 3 weeks' duration; 6 were treated with aspiration; and 1 required the insertion of a tube with water-seal drainage after failure of the lung to reexpand on bed rest alone. Five of the 25 patients so far have undergone a corrective surgical procedure. One had a local resection of the single cyst; the other 4 patients had segmental or wedge resections of the involved area and a parietal pleurectomy; 1 of the 4 had this procedure performed on both sides; all 4 were returned to flying status after recovery.

The primary concern in flying personnel who have a spontaneous pneumothorax is the possibility of complete collapse of the involved lung and/or the development of a tension pneumothorax. Either complication could severely compromise the ventilatory function of the remaining lung and could embarrass cardiovascular hemodynamics. Corrective surgery in the form of segmental or wedge resection of the diseased area and parietal pleurectomy will minimize the possibility of a recurrence and of complications.

Familial Patterns in Hypertension and Coronary Heart Disease. C. B. Thomas. Circulation 20:25-29 (July) 1959 [New York].

The author embarked in 1946 on a long-term investigation of the genetic factors of hypertension and of coronary heart disease among the parents and grandparents of 724 Johns Hopkins medical students. Approximately 11% of the fathers and 14% of the mothers were reported to have hypertension, while 9% of the fathers and 2% of the mothers had coronary disease. Ten per cent of the students had

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The place of publication of the periodical appears in brackets preceding each abstract.

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a parent with questionable hypertension or coronary disease. Therefore, less than two-thirds of the students have had both parents free from either disorder. Comparing the findings among the parents and grandparents, the greatest proportion of affected persons with hypertension was found among the offspring of 2 affected parents, and the smallest proportion among the offspring of 2 unaffected parents with hypertension. A similar genetic correlation was observed for coronary disease.

While the most marked correlation was observed when the prevalence of the same disorder was studied in 2 successive generations, similar but less striking correlations were found when hypertension was investigated in one generation and coronary disease in the other. Certain sex differences in the familial appearance of hypertension and coronary disease were noted in this series. The female relatives of hypertensive women were found to have more than twice as much hypertension as their male relatives, while the male relatives of hypertensive men had almost twice as much hypertension as their female relatives. These findings support the hypothesis that hypertension and coronary heart disease are at least partly hereditary disorders.

Lung Volume in Smokers and Nonsmokers. H. Blackburn, J. Brozek and H. L. Taylor. Ann. Int. Med. 51:68-77 (July) 1959 [Lancaster, Pa.].

Since tobacco smoking has long been suspected as an etiological factor in respiratory symptoms and in chronic bronchopulmonary disease, the authors made lung volume measurements on 221 business and professional men of Minneapolis and St. Paul. These men participated in a 10-year longitudinal study of cardiovascular aging. The age range at the time of lung volume measurement was 47 to 57 years—mean age, approximately 52 years. The subjects were selected from 916 acceptances to 1,000 invitations, issued in cooperation with several Twin Cities' business, industrial, and professional organizations, and were randomly chosen to fill categories of different relative body weights. Questionnaires on smoking, comparable to those of the American Cancer Society, were analyzed, and classification of cigarette smoking habits was made according to the following criteria: "never"; "occasional" (not daily); "light" (1 to 10 cigarettes daily); "moderate" (10 to 20 cigarettes a day); "heavy" (over 20 cigarettes a day); and "stopped" (for at least a year).

It was found that vital capacity was smaller in each category of smokers. The difference from nonsmokers reached a statistically significant level for all smoking categories combined. Residual lung volume was larger in all categories of smokers, but not consistently at significant levels statistically. Total lung capacity was not significantly different between groups. The ratio of residual volume to total lung capacity (RV/TLC × 100) was significantly greater in smokers. In a group which had successfully stopped all smoking, the lung compartment values were similar to those of a group who had never smoked, and the RV/TLC was significantly smaller than in the current smokers. Stringent screening of this sample for abnormal respiratory manifestations left a residual 188 men in whom the same order of differences in lung volume prevailed between smokers and nonsmokers as in the total sample. The prevalence of an "elevated" (> 35%) residual volume/total lung capacity ratio was significantly greater in smokers. Differences in vital capacity, residual volume, and RV/TLC were in the direction to be expected if smoking is a factor in producing a functional increase of airway resistance. Comparable differences in lung volume have been found by others in a population examined with reference to smoking habit.

Portal Hypertension and Bleeding Esophageal Varices: Their Occurrence in the Absence of Both Intrahepatic and Extrahepatic Obstruction of the Portal Vein. W. A. Tisdale, G. Klatskin and W. W. L. Glenn. New England J. Med. 261:209-218 (July 30) 1959 [Boston].

Within the past 8 years the authors encountered at the Grace-New Haven Community Hospital in New Haven, Conn., 5 patients with bleeding esophageal varices and portal hypertension in the absence of demonstrable intrahepatic or extrahepatic venous obstruction. One of the 5 did not have a satisfactory splenoportogram, but the other 4 underwent complete clinical, radiologic, and surgical investigation and constitute the basis for this report. The first patient was a 23-year-old man, who had experienced several bouts of massive gastrointestinal hemorrhage, presumably from large esophagogastric varices, in the 5 years before shunt surgery. A splenoportogram and careful inspection at laparotomy demonstrated a patent, somewhat dilated portal system with elevation of the portal pressure. Two liver-biopsy specimens, obtained 2 years apart, demonstrated only small and inconstant zones of periportal congestion, with no apparent progression or alteration in the 2-year interval. Serial liver-function tests failed to indicate significant hepatic dysfunction.

The second patient was a 58-year-old man. Here again portal hypertension was demonstrated in the absence of both intrahepatic and extrahepatic portal vein block. In the third patient, a 72-year-old man, neither clinical studies nor postmortem examination indicated a cause of increased resistance to flow within the portal bed. The minimal periportal hepatic fibrosis did not seem extensive enough to distort intrahepatic portal radicles and may have been secondary to the increased portal tension itself. The fourth patient was a 10-year-old girl, who presented with massive hematemesis and palpable splenomegaly. The past history of a febrile neonatal illness, associated with splenomegaly, suggested that septic inflammation of the portal vein, perhaps from omphalitis, had led to subsequent portal thrombosis, portal hypertension, congestive splenomegaly, and the development of varices. Although portal hypertension was confirmed by direct measurement at operation, a splenoportogram and surgical exploration failed to demonstrate any obstruction to the portal outflow, either outside or within the liver.

Increased portal blood flow seems the most likely cause of the venous hypertension in these patients. Although gross arteriovenous anastomoses involving the splenic and portal veins were not found, functional or structural alterations of the vessels of the gastrointestinal tract, the spleen, and the liver may have permitted increased flow of blood into the portal vein, with a resultant rise in pressure. Despite the compensatory dilatation of the main portal vessels and the opening of numerous venous collaterals, portal pressures remained elevated, with the eventual production and rupture of esophageal varices. The combination of a normal, or near normal, liver-biopsy specimen and an unobstructed portal vein in a patient with bleeding esophageal varices secondary to portal hypertension should lead to investigation of the factors affecting portal blood flow. Of considerable help would be the direct measurement of blood flow through the portal vein tributaries at the time of laparotomy. Another approach might be the differential temporary occlusion of arteries supplying organs drained by the portal vein, thereby localizing any abnormal arteriovenous unions. Careful postmortem perfusion studies of the liver, spleen, and gastrointestinal tract of such patients might reveal alterations in the structure and function of these blood vessels.

Serious Complications of Peptic Ulcer After Acute Myocardial Infarction. J. C. Shipp, V. W. Sidel, R. M. Donaldson Jr. and S. J. Gray. New England J. Med. 261:222-226 (July 30) 1959 [Boston].

Myocardial infarction may be associated with an increased gastric secretory response and activation or appearance of peptic ulcer. The histories of 6 patients with serious complications of peptic ulcer during the acute phase of myocardial infarction are reported. Perforation occurred in 4, and bleeding in 2. These complications present special problems in management. Emphasis should be on prevention. It is recommended that a patient with acute myocardial infarction, together with past or present symptoms suggestive of ulcer, receive an ulcer regimen prophylactically, and that anticoagulants be withheld or used with extreme caution.

There is evidence of a relation between adrenocortical activity and ulcer formation. The authors investigated the urinary excretion of 17-ketosteroids, 17-hydroxycorticoids, and uropepsin in 10 consecutive patients admitted to the Peter Bent Brigham Hospital in Boston with an acute myocardial infarction. Each of the 10 patients showed the clinical, electrocardiographic, and laboratory changes documentary of acute infarction. A control group included 10 patients with known coronary-artery disease but without recent myocardial infarction, who were hospitalized because of congestive heart failure or angina. No patient in either group had a history of peptic ulcer disease. In 4 of the 10 patients with acute myocardial infarction, the uropepsin excretion was elevated. In all 4 this returned to the normal range during convalescence. Of the control group of 10 patients, none had an elevated uropepsin. There was no demonstrable difference in the adrenal response in the 2 groups. It is suggested that, in certain cases, a myocardial infarction may constitute an acute ulcerogenic stimulus.

The High Incidence of Peptic Ulcer in Obstructive Emphysema with Cor Pulmonale. M. L. Gottlieb. Santo Tomas J. Med. 14:1-10 (Jan.-Feb.) 1959 (In English) [Manila, Philippines].

It is becoming more and more apparent that in the pathogenesis of disease the main organ involved may represent the end-process of a disturbed pathological-physiological entity. The finding of bleeding ulcers at the autopsy of a patient who had been admitted to the Whipple VA Hospital in Manila with a diagnosis of decompensated cor pulmonale was the initial factor in the investigation reported by the author. The patient, a 64-year-old man, had been hospitalized before at the same hospital without ever showing any gastrointestinal sign or symptom. After his death it was considered advisable to perform a gastroscopic examination on all patients suffering from cor pulmonale or pulmonary emphysema. In a group of 65 such patients, radiologic examination disclosed that 7 had gastric ulcer; 10, duodenal ulcer; and 5, both gastric and duodenal ulcers. The gastric ulcers were mainly in the prepyloric region of the lesser curvature. Twenty-five other patients had gastritis of varied degrees of severity. Gastroscopy was performed on 13 of these 25 patients, and in 9 of them it showed hypertrophic gastritis. Only a few of all the patients with gastrointestinal positive findings had shown any clinical signs or symptoms of this type of disorder.

The clinical findings concerning this group of patients were compared with 65 records concerning cases of pulmonary emphysema or cor pulmonale, taken from the protocols of autopsies performed at the Whipple VA Hospital between 1948 and 1955. The patients described in these records were all male, with an average age of 56 years. Gastroduodenal pathology was described in 27 of these 65 records. Ten patients had had gastric ulcer, and 11 had had duodenal ulcer, while 6 had suffered from hypertrophic gastritis. Seven of the patients with gastroduodenal trouble had died of massive hemorrhage, and 2 of hemorrhage and perforation. Only in 3 cases of gastroduodenal disorder associated with cor pulmonale or pulmonary emphysema had the gastroduodenal condition been diagnosed and treated for any appreciable length of time prior to death. Several mechanisms may account for the association of peptic ulcer with cor pulmonale and pulmonary insufficiency; increased production of histamine may be one of the most important factors. Irrespective of the causative factor, it is important that patients suffering from cor pulmonale or pulmonary insufficiency be given a thorough gastroduodenal examination. It is also imperative that the administration of adrenocortical extracts and of reserpine to this group of patients be controlled very carefully, given their greater eligibility for the production of ulcerative lesions in the stomach or duodenum.

Accidental Swallowing of a Partial Denture and Its Spontaneous Passage Through the Gastrointestinal Tract. W. Furste and P. Watkins. Am. Surgeon 25:486-488 (July) 1959 [Baltimore].

A 26-year-old woman sneezed and swallowed a partial denture, which consisted of 2 teeth, a metallic support, and a sharp clasp at each end. Operative intervention was considered, primarily because of the projecting sharp points of the denture and not because of the size of the object. Fear was entertained that these sharp points might penetrate the gastrointestinal tract at the pyloric or ileocecal valves or at the duodenal or duodenojejunal curvatures. With conservative management, however, the partial denture moved slowly through the gastrointestinal tract, and, 6 days after being swallowed, it was found enclosed in a mass of feces.

Studies on the Oral and Parenteral Administration of D (+) Xylose. C. E. Butterworth Jr., E. Perez-Santiago, J. M. de Jesus and R. Santini. New England J. Med. 261:157-164 (July 23) 1959 [Boston].

The absorption of xylose by the mammalian intestine was studied by Cori in 1925, and has recently received attention in connection with studies of malabsorption syndromes. The low levels of xylose absorption reported by Cori were later attributed to the fact that he used L-xylose, which is absorbed much more slowly than its isomer, D-xylose. Other investigators substituted D-xylose in testing renal function and found that the urinary excretion of this pentose is proportional to the plasma concentration and is independent of the volume of urine flow. The authors present the results of oral and intravenous xylose tolerance tests and describe certain tests of xylose absorption and metabolism in laboratory animals. Commercial D-(+)-xylose (Pfanstiehl or Fisher), reagent grade, was used in all studies. A 25-Gm. dose was dissolved in 250 ml. of tap water and administered orally to fasting subjects. The glass was filled with another 250 ml. of water and administered to assure ingestion of the entire dose and to provide water for adequate urine flow. All urine excreted during the next 5 hours was collected. Xylose for intravenous administration was prepared as a 20% concentration (weight volume) in isotonic sodium chloride solution. Solutions were sterilized by autoclaving.

In a series of 114 normal subjects, the 5-hour urinary excretion of xylose after a 25-Gm. oral dose was found to be 5.7 Gm. (mean) ± 1.4 Gm. (S. D.). A result of less than 3 Gm. was presumptive evidence of malabsorption, low xylose results correlating well with other absorption tests. The test was simple, reproducible, and accurate and caused a minimum of inconvenience to the patient. In the presence of normal renal function, blood samples were not required, and venepunctures were avoided. Patients with sprue in relapse consistently showed diminished urinary xylose excretion. In 49 such subjects the mean excretion was 1.4 Gm. in 5 hours. Treated patients showed excretion values ranging from low to normal, with a mean value of 3.5 Gm. Low values were sometimes encountered in certain other megaloblastic anemias and in other malabsorption syndromes. Administration of xylose by the intravenous route to normal persons and patients with sprue resulted in excretion of approximately 11 Gm. in 24 hours in all subjects. This supports the contention that malabsorption accounts for the low excretory rate observed in patients with sprue after the oral administration of xylose.

Studies with normal laboratory animals indicated ready absorption of xylose by the intestine. Significantly more xylose was excreted with parenteral administration than with oral administration. It was not possible, though, to demonstrate chemically an increase in rat liver glycogen after xylose administration. The simplicity and accuracy of the xylose test commend it for more widespread use in the diagnosis of malabsorption syndromes.

Diverticulum of the Gallbladder: A Report of Three Cases and a Review of the Literature. J. P. Arcomano and J. C. Barnett. Am. J. Digest. Dis. 4:556-562 (July) 1959 [New York].

Congenital gallbladder diverticula are referred to as true diverticula of the gallbladder and must be differentiated from acquired diverticula. The differentiation can be made on the basis of the histological features of each when pathological specimens are available. True congenital diverticula retain all the histological features of the gallbladder; roentgenographically, they will become apparent and will contract normally after a motor fatty meal in the absence of any secondary condition. Acquired diverticula, except the traction type, do not usually retain the histological features of the gallbladder. It is apparent from the literature that there are usually associated factors that predispose to the formation of acquired diverticula. These can be in the nature of a traction diverticulum or in the form of a partially healed gallbladder fistula which may simulate a diverticulum in its projection from the gallbladder. Intramural diverticulosis may develop, having its origin secondary to chronic obstructive condition of the gallbladder, with resultant increased intracystic pressure. Finally, finger-like sinuses may project through defects in the muscularis mucosae to produce multiple pseudodiverticula or a single diverticulum. It is evident, from the etiological factors, that acquired diverticula cannot contract normally after a motor fatty meal because of inhibition by mechanical traction factors or because there is no normal muscularis mucosae present within the pseudodiverticula to respond to a normal stimulus. The authors report on 3 women with a diverticulum located in the fundus of the gallbladder. Physical examination of these 3 patients was noncontributory, but a later gastrointestinal survey revealed the presence of a diverticulum.

Gaucher's Disease: Report of Two Cases in Father and Son and Review of the Literature. D. Yi-Yung Hsia, J. Naylor and J. A. Bigler. New England J. Med. 261:164-169 (July 23) 1959 [Boston].

Gaucher's disease (also known as lipid histocytosis of kerasin type) is a rare hereditary metabolic disorder, some 300 cases having been reported since the condition was first described by Gaucher in 1882. The authors briefly describe an "adult" form and an "infantile" form of the disease. The typical Gaucher cell is a large cell, 20 to 80 μ wide, whose cytoplasm is light blue in Giemsa-stained preparations. There are fine fibrils in the cytoplasm, giving a wrinkled rather than a foamy appearance. The cells are polymorphous and may have projections or be stretched. The nucleus is small, pyknotic, and usually eccentric, and may be multiple. There is controversy over whether they are reticulum cells or are of endothelial origin. Gaucher cells are best demonstrated in the spleen, liver, and bone marrow. At least 3 substances have been isolated in normal quantities within the tissues containing Gaucher cells: a galactosiderocerebroside (kerasin), which is composed of lignoceric acid, sphingosine, and galactose; a glucosiderocerebroside, in which the hexose is present in the form of glucose instead of galactose; and a water-soluble glycolipid, which is made up of long-chain, saturated fatty acids, sphingosine, or a sphingosine-like base and one or more hexose residues. The last type of compound has been named a "polycerebroside." The explanations suggested for the disease are briefly discussed, and its familial occurrence is mentioned.

The cases presented concerned a 1-year-old boy and his 42-year-old father. In both patients the diagnosis was verified by the detection of typical Gaucher cells in the bone marrow. The authors undertook a survey covering most of the cases of Gaucher's disease reported in the literature. A total of 110 families were found. A superficial analysis suggests that the clinical entity known as Gaucher's disease may represent at least 3 genetically distinct groups: in a few families, the condition is transmitted by an autosomal dominant gene; in the majority, it is caused by an autosomal recessive gene; and, in a third group, there is always neurological involvement in addition to the usual changes in the bone, liver, and spleen, and the condition also appears to be transmitted by an autosomal recessive gene. At the present time, it is not known whether these genes represent a system of separate alleles having one locus, or are located at separate loci.

Hepatic Coma Associated with Acute Viral Hepatitis: Recovery with ACTH: Report of One Case. H. P. MacCubbin. Virginia M. Month. 86:414-416 (July) 1959 [Richmond].

The case of a 16-year-old youth in coma subsequent to hepatitis, who recovered after corticotropin (ACTH) was added to the therapeutic regimen, is presented. Six weeks prior to hospitalization the patient suffered from headache, vomiting, and deepening icterus. Examination on admission revealed a normally developed but deeply jaundiced, moderately cachectic, and quite dehydrated boy, who was lethargic and vaguely responded to questioning. Rectal temperature was 100 F; pulse, 60 per minute; and respiration, 16 per minute. The abdomen was slightly distended. The liver could be easily palpated 4 cm. below the costal margin and was smooth and tender. The spleen was not palpable. Treatment began with bed rest and dietotherapy with vitamin supplement including brewers' yeast and vitamin B complex. Pain in the region of the liver and vomitus (containing blood) precluded oral therapy. The parenteral administration of dextrose and electrolytes with vitamin supplement was started on the third day of hospitalization. Small amounts of meperidine (25 mg.) were given by injection for pain and restlessness; Kappadione was also administered intravenously. The abdominal fluid, however, increased in amount, and presacral edema of mild degree was noted. After salt had been removed from the diet, Thiomerin (1 cc.) was administered subcutaneously.

On the 5th day of hospitalization the patient became comatose, and his condition appeared hopeless. It was then that the administration of ACTH (plain) was begun, 25 units being given intramuscularly every 6 hours, with very good results. In 4 days the youth was able to receive an adequate amount of fluids and other nutriments orally, and after 2 more days he was fully alert and cheerful and had an excellent appetite. The dose of ACTH was gradually decreased, and then discontinued after 5 days. On the patient's discharge a month later, the liver edge could be felt 2 cm. below the rib margin, firm and nontender. The white blood cell count had also increased, and at the last follow-up the liver edge was barely palpable on deep inspiration.

The mechanism of action of ACTH and corticosteroids in case of coma due to acute viral hepatitis is still unknown. A theory suggesting pituitary suppression in advanced liver disease on the basis of known decrease in 17-hydroxycorticoid output has been advanced. The author believes that ACTH and adrenocorticoids should be added to the usual therapeutic regimen when the latter stage of sensorial disturbance is reached.

Staphylococcal Septicemia: A Review of 30 Cases. W. J. Holloway and E. G. Scott. Delaware M. J. 31:198-203 (July) 1959 [Farmhurst].

The authors present a clinical review of 32 episodes of staphylococcic septicemia in 30 patients observed during the past 3 years at the Delaware Hospital in Wilmington. Of the 32 episodes of staphylococcic septicemia, 20 were hospital-acquired infections and 12 were non-hospital-acquired. Eleven of the patients who acquired the infection from the hospital environment died, whereas only 2 of those with infections acquired prior to hospital admittance died. Seven of these 13 deaths occurred in 10 patients who contracted the infection during the last year of this study, thus revealing an alarming increase in mortality. All the patients had at least a single isolation of a coagulase-positive Staphylococcus aureus from the blood stream. The most frequently recovered hospital strains were resistant to penicillin, to tetracycline, and, in 8 instances, to erythromycin. The organisms isolated from the 12 patients who were already infected on admission showed a lower order of resistance. Leukocytosis was a consistent finding in the patients in this study. Of 53 courses of therapy, good results were obtained 18 times; poor results, 29 times; and indeterminate results, 6 times. The correlation between the in vitro sensitivity of the organisms and their in vivo sensitivity and the in vivo response to the antibiotic was excellent. In 5 cases of septicemia in which antibiotics had failed, cures were effected by surgical drainage of amenable foci of infection.

It is suggested that therapy be instituted immediately when septicemia due to staphylococci is suspected in a hospitalized patient. Intravenously administered vancomycin should be given in doses of 1 or 2 Gm. per day. If the intravenous route is not feasible, neomycin or kanamycin may be given intramuscularly. Both of the latter drugs are toxic to the 8th nerve and should not be used in the presence of impaired renal function, unless the renal damage itself is a result of the staphylococcic infection. Chloramphenicol and novobiocin should not be used individually in the treatment of staphylococcic septicemia. When used together, or singly in combination with erythromycin, good therapeutic results may be expected. However, the authors' experience with these essentially bacteriostatic agents in the treatment of severe staphylococcic infection has been disappointing. It is emphasized that, if an organism is susceptible to penicillin, this drug is certainly the antibiotic of choice. Among important measures which should bring about a reduction in mortality from staphylococcic septicemia are: (1) isolation of the infected patient; (2) protection of the highly susceptible patients; (3) scrupulous aseptic and antiseptic practices; (4) cessation of indiscriminate and prophylactic antibiotic therapy; and (5) awareness of the problem by the medical profession.

Immediate Results of Treatment of Advanced Malignant Tumors with Combined Chemotherapy and Hormones in High Doses. J. Ramos Jr., E. Parisi, A. C. C. Junqueira and others. Rev. paulista med. 54:335-340 (May) 1959 (In Portuguese) [São Paulo, Brazil].

Forty-five patients with advanced cancer of different types and localization received a combined chemical and hormonal treatment on the chemotherapy service of the Associação Paulista de Combate ao Cancer in São Paulo, Brazil. The treatment started with the administration of corticotropin (ACTH) and prednisone, given intramuscularly in daily doses of 240 to 300 mg. It included oral therapy with Meticorten, 100 mg. a day, and with Omcilon, 40 mg. a day. These doses, administered in association with nitrogen mustard (Dichloren), were reduced gradually. Dichloren was administered in the daily dosage of 0.1 mg. per kilogram of body weight for periods of 5 consecutive days. Two patients received this dosage for periods of 10 consecutive days. In 4 cases the administration of triethylene melamine (TEM) was also included. Antibiotics and blood transfusions were part of the general therapeutic plan according to individual needs.

The results of the combined treatment were termed very good in 14 cases. These patients experienced relief of their symptoms, decrease of the tumor size, and, in some cases, a return to normal life. Their survival was longer than 3 months. The tumors which responded best to the therapy were ovarian and lung. There were fair results in 13 cases. These patients experienced at least a subjective improvement for about one month. In 9 patients the condition remained unchanged, and in the other 9 it continued a downhill course. In addition to these results, there was less depression of the bone marrow than is usually the case with the administration of alkylating drugs. The side-effects were rather mild and easily controlled.

SURGERY

Surgery of Cerebral Hemorrhage: Report of the Results of 52 Surgically Treated Cases. G. Lazorthes. J. Neurosurg. 16:355-364 (July) 1959 [Springfield, Ill.].

The author reports the results of surgical treatment in 52 cases of intracranial spontaneous hematoma, omitting cases in which the intracerebral bleeding was the result of trauma or tumor, or was secondary to vascular malformations. The distinction between cerebral hemorrhage and cerebral hematoma is not clear-cut. It has been stated that cerebral hemorrhage occurs in elderly hypertensive-arteriosclerotic patients, whereas cerebral hematoma is met with in a relatively younger age group, presenting no significant signs of arteriosclerosis. In fact, neither the etiology nor the pathogenesis can be considered as sound criteria for differentiation. It has also been said that cerebral hemorrhage is deep-seated and infiltrates the brain, whereas cerebral hematoma is located in a cerebral lobe, but the starting point of the bleeding is no proof in favor of the type of the lesion.

In the author's opinion, hemorrhage takes its source more often from the central or capsulostriate blood vessels; what is of most significance is the extravasation of blood toward the cortical centers or within the white matter of the brain at the junction of central and peripheral arterial territories. The classical type of capsular hemorrhage often tears the internal capsule, compresses the diencephalic centers, and may invade the ventricles of the brain. From the internal or external capsule the hemorrhage may extend into the white matter of the cortex: in the frontal or in the temporal lobes; more frequently in the parieto-occipital region. It collects itself into a hematoma. The parieto-occipital location of the hematoma in the region proximal to the ventricle is by far the most frequent; it accounted for nearly 75% of the cases observed by the author.

The decision to intervene surgically rests on increase in severity of symptoms and on the exact location of the hematoma. Angiography is the conclusive examination, because the diagnosis, the localization of the hematoma, and the explanation of the etiology depend on its findings. Moreover, it dictates the surgical procedure. In the subacute and pseudotumoral forms in young or middle-aged patients, with no signs of arteriosclerosis and no hypertension, the surgical approach is mandatory. In acute or superacute forms in older arteriosclerotic patients with cardiovascular symptoms or impaired renal function, or in cases of massive capsular hemorrhage the decision has to be carefully weighed. Results obtained justify operation in a high percentage of cases.

Hypertension existed in 29 of the patients with cerebral hematoma reported. In this group there were 10 complete recoveries; 11 patients recovered but had sequels, such as paralysis, paresis, or hemiopia; death occurred in 8. In 20 patients of a younger age group than those with hypertension, who had no signs of vascular lesions, there were 7 complete recoveries with no neurological deficit and 13 recoveries with neurological residuals. There were 2 cases of hematoma secondary to subacute bacterial endocarditis; one patient had a complete recovery, and the other died on the 5th postoperative day of heart failure. There was one case of hematoma probably secondary to blood dyscrasia in an alcoholic patient, who recovered with a persistent residual hemiplegia.

Time Studies of Acute, Reversible, Coronary Occlusions in Dogs. S. Yabuki, G. Blanco, J. E. Imbriglia and others. J. Thoracic Surg. 38:40-45 (July) 1959 [St. Louis].

The surgical management of coronary occlusion has been directed toward relief of chronic myocardial ischemia by means of revascularization procedures. In the past, the indirect approach to revascularization has predominated with grafting of various tissues onto the myocardium (omentum, lung, pectoral muscle), implantation of systemic arteries into the heart musculature, abrasion of the epicardium, and arterialization, or merely constriction of the coronary sinus. Lately, the direct attack on the constricting lesion, by endarterectomy or by excision and replacement of the diseased segment, has made its appearance. Once the feasibility of the direct approach is accepted, the applicability of similar direct measures on the acutely obstructing process, that is, the emergency surgical treatment of the acute coronary occlusion, can be considered. An essential factor in establishing the effectiveness of such a policy would be to ascertain the available time during which emergency relief of an acute complete occlusion would result in preventing death of the myocardium. Should this time be commensurate with the interval needed for diagnosis, for transportation of the patient to a surgical facility, and for performance of an emergency operation, such a policy would have a rational basis.

In order to determine the critical period during which emergency relief of the complete occlusive process would be curative, the authors made experiments on animals. Dogs, weighing between 12 and 20 kg. (27 and 44 lb.), were anesthetized with intravenously administered Pentothal, intubated, and connected to a mechanical respirator; oxygen was administered throughout the procedure. The left common carotid artery was cannulated, and continuous blood pressure was recorded thereby. A thoracotomy was performed, and after incising the pericardium and securing it to the chest incision, the anterior descending branch of the left coronary artery was dissected free, care being taken to avoid trauma to its branches or to the accompanying veins. A braided silk ligature was then passed around the artery, and both ends were threaded through soft plastic tubing in order to provide a tourniquet. In some of the dogs the same procedure was employed at other sites along the course of the anterior descending artery or its 2 main branches.

The tourniquet was then tightened, occluding the artery completely, as evidenced by distal collapse of the vessel and appearance of a cyanotic area corresponding to its distribution. Drying of the myocardial surface was prevented by moistening it with warm saline solution. A record was kept of the myocardial action and color, blood pressure, and condition of the corneal reflex. After a definite period, the occlusion was terminated, the silk ligature was removed, and the pericardial and chest incisions were closed. Electrocardiographic recordings of the 3 standard leads were obtained before opening the chest, during and after occlusion, and after chest closure. They were repeated at the time of killing, which varied between 48 hours and 14 days after the operation. At the killing, the heart was excised. Twenty hearts were examined microscopically, the investigators noting the condition of the myocardium supplied by the temporarily occluded artery, and examining the vessel itself for evidence of permanent damage or of postoperative thrombotic phenomena. The evidence obtained indicates that a complete occlusion lasting for more than 45 minutes will produce the irreversible changes characteristic of myocardial infarction.

A Critical Evaluation of Direct Surgical Procedures in the Treatment of Occlusive Peripheral Vascular Disease. O. Creech Jr., R. J. Schramel and K. Reemtsma. Am. Surgeon 25:492-497 (July) 1959 [Baltimore].

The authors summarize the results of operations on 65 patients with occlusive peripheral vascular disease, 24 of whom had aortoiliac disease and 41 had occlusion involving the femoral and popliteal arteries. Two types of procedures were employed, namely, bypass grafting and thromboendarterectomy, or, more properly, thrombointimectomy. Crimped nylon grafts were used almost exclusively for bypass operations. Of the 24 patients with aortoiliac occlusion, 14 were treated by grafting. Of these 14 grafting operations, 12 were immediately successful in that there was restoration of blood flow with palpable pulses in the lower extremities. Of the 12 functioning grafts, 1 subsequently became infected and was removed, and in 2 patients the graft became occluded about 6 months after implantation. The remaining 9 patients have had significant improvement in their symptoms, and restoration of blood flow to the lower extremities has been maintained for periods varying from 6 months to 2 years. There were 2 deaths in this group. Thrombointimectomy was performed on 10 patients with aortoiliac occlusion. All these operations restored blood flow, and there have been no late failures in this group.

Of the 41 patients with femoral-popliteal occlusions, 26 were treated with grafts. Twenty of the procedures were immediately successful in that blood flow was restored, as indicated by palpable pedal pulses, relief of symptoms, and healing of necrotic areas. However, in 15 cases the grafts are known to have become occluded at periods ranging from 6 months to 2 years; 2 patients could not be followed, and in 3 the grafts are still functioning after periods of from 9 to 18 months. Of the 15 patients with femoral-popliteal occlusions treated by thrombointimectomy, the operations were immediately successful in 11 and unsuccessful in 4. In 2 of the 4 failures the bypass operation had also been unsuccessful. Among the 11 patients in whom thrombointimectomy was initially successful, no subsequent occlusion has occurred during periods of observation ranging from 2 to 18 months. Because of the frequency of late closure of bypass grafts, it is believed that thrombointimectomy is the preferable method of treatment in occlusive peripheral vascular disease.

Perforated Duodenal Ulcer During Steroid Therapy: Report of Four Cases, Including Two Giant Perforations. B. F. Benton and E. Bramlitt. Am. Surgeon 25:482-485 (July) 1959 [Baltimore].

The first of the 4 patients reported was a 39-year-old woman who had been treated for rheumatoid arthritis for 20 years and during the past few months had received 10 mg. of prednisone daily. Several months before admission she began to have tarry stools. Gastrointestinal examinations revealed a duodenal ulcer, and ulcer therapy was instituted. The onset of severe epigastric pain with rigidity of the abdomen and vomiting induced the authors to make a roentgenogram of the abdomen in the lateral decubitus position. When this revealed free air in the peritoneal cavity, a tentative diagnosis of perforated duodenal ulcer was made, and laparotomy was performed. A giant duodenal ulcer had perforated into the peritoneal cavity. This perforation was 3.5 cm. in diameter, and it involved the lateral and anterior wall of the first portion of the duodenum. A two-thirds subtotal gastrectomy was performed with an anterior Hofmeister anastomosis. The patient had an uneventful postoperative course. She was on maintenance therapy with steroids during the postoperative course and after discharge from the hospital. Follow-up in the outpatient department revealed that she was getting along well and was free of ulcer symptoms.

The second patient, an 11-year-old girl, was given at first 15 mg., and later 10 mg., of prednisolone after a diagnosis of dermatomyositis had been made. After several weeks of treatment she complained of abdominal pain, and a diagnosis of perforated peptic ulcer was made. At laparotomy she was found to have a 3-mm. perforation in the anterior wall of the duodenum. This was closed. The patient had an uneventful postoperative course. She was gradually weaned from her steroid therapy during the next month, and was discharged from the hospital in good condition.

The remaining 2 patients died. One was a 41-year-old woman, who had bilateral pleural effusions due to metastatic carcinoma of the breast. The patient had been on prednisone therapy, 10 mg. daily, for 2 months, as well as on testosterone. Radical mastectomy had been performed 2 years, and oophorectomy 17 months, previously. Autopsy revealed a 1-cm.-wide ulcer in the first portion of the duodenum, with the gallbladder adherent to the perforation. No evidence of generalized peritonitis was present. The other patient who died was a 6-year-old boy, who was being treated with prednisolone for the nephrotic syndrome. A diagnosis of perforated peptic ulcer was made, but because of his critical condition it was decided that nonoperative treatment should be carried out. He died, and autopsy revealed, among others, an atypical picture of acute glomerulonephritis, marked ascites, and a 3-by-4-cm. subhepatic abscess on the right. A large (2 by 3 cm.) perforated duodenal ulcer was found on the posterior aspect of the duodenum.

Patients who are to be treated with any type of corticosteroid therapy should have an upper gastrointestinal series done in order to rule out a duodenal ulcer. If there is a history of peptic ulcer or if the gastrointestinal series demonstrates ulceration, it is usually advisable to withhold these drugs. Once perforation has occurred, it may be necessary, during and immediately after surgery, to give larger doses than the patient had been taking before surgery. Surgical intervention is urged in perforated ulcers in these patients when possible, since a giant perforation may be present and will not "seal" itself readily. Primary gastric resection should be considered in patients on long-term steroid therapy undergoing surgery for perforated duodenal ulcers.

Intestinal Diverticula. J. K. McCollum. Brit. M. J. 2:34-38 (July 11) 1959 [London].

The author reports on 7 women and 3 men with uncomplicated diverticula of the duodenum, whose average age was 52 years. Two of these patients had hematemesis and melena. The cases of 2 additional patients, one a 65-year-old woman with fatal hemorrhage from a jejunal diverticulum, and the other a 66-year-old woman who recovered after resection of a segment of the upper jejunum for acute diverticulitis and had to be readmitted to hospital for hematemesis, are described. Ninety patients with diverticula of the colon and one patient with acute diverticulitis of the cecum were studied. The commonest presenting complaint of the patients with diverticulosis was that of recurrent episodes of abdominal pain, accompanied in those with duodenal and jejunoileal diverticulosis by flatulent dyspepsia, and in patients with diverticula of the colon by alteration in bowel habit.

The high incidence of diverticula found simultaneously in several segments of the intestine denotes that it is a disease of the whole intestine, although the occurrence of a complication may direct attention mainly to one segment. Surgical intervention, other than that necessary for relief of an existing complication, would be advisable only in patients in whom it could be shown that a serious complication was likely to occur. Such intervention would not prevent progress of the disease or development of later complication at a different level in the intestine. It is doubtful if uncomplicated duodenal diverticula even require active surgical treatment. Operation may be necessary in patients with uncomplicated jejunal diverticula, particularly if the dyspepsia is accompanied by obstructive features. The demonstration of duodenal or jejunal diverticula may be regarded as an adequate explanation for chronic or recurrent dyspepsia, provided that precautions have been taken to exclude other active lesions.

Of the 90 patients with diverticula of the colon, 61 had recurrent attacks of abdominal pain, painless diarrhea, or signs of pericolitis without frank pus formation; follow-up examinations after 4 years showed, however, that, with one exception, there had been no deterioration in any of them. The fact that perforation of a diverticulum, i. e., a serious complication, occurred in one patient emphasizes the risks these patients are subject to but does not provide a mandate for prophylactic resection of the colon. The 2 most important complications of diverticulosis of the colon observed have been diffuse peritonitis, secondary to acute perforation of a diverticulum, and acute suppurative pericolitis. Careful clinical assessment, sigmoidoscopy, and roentgenograms are necessary after recovery from the acute illness and before a final decision is made. Proximal colostomy should be performed on most of the patients with perforation of the colon: experience has shown that this may be closed after recovery from the acute illness. The later prognosis for patients who recover from a perforated diverticulum is good.

The causes of death in 4 paitients with acute suppurative pericolitis were toxemia and exhaustion in 1 patient, diffuse peritonitis in 2 patients, and suppurative pylephlebitis in 1 patient. Autopsy in all of them showed widespread suppuration and necrosis in the pericolic and retroperitoneal tissues. Surgical exploration should be undertaken early in patients with this condition, before the likely onset of such complications as pylephlebitis; if the findings are such that simple drainage will not be effective, the diseased colon and the surrounding infected tissues should be removed. No attempt should be made, however, to reestablish intestinal continuity by simultaneous anastomosis.

Carcinoma of the Colon in Young People. F. W. Chappell. Am. Surgeon 25:449-457 (July) 1959 [Baltimore].

Chappell aims to bring up to date the information about carcinoma of the colon in young persons and to present 2 new patients, a 16-year-old girl and a 14-year-old boy, who were treated for carcinoma of the colon at the Baptist Memorial Hospital in Memphis, Tenn., within the past few years. Data on 88 young patients collected from the literature (including the 2 recently observed by the author) are tabulated. The review includes only patients who were less than 20 years old, and in whom the carcinoma was located in the portion of the colon above the rectosigmoid. The greatest number of cases occurring in the first 2 decades of life are in the 10-to-14-year age group. This would seem to be related to the increased growth rate and other physiological changes normally occurring at the age of puberty. Cancer of the colon (excluding the rectum) is slightly more common in females among adults, but it has been found to occur more frequently in males below the age of 20. Of 84 patients for whom the sex was indicated in the series reported, 58 were males.

The portion of the colon most commonly affected by carcinoma is the sigmoid, the site of 24 of the 78 lesions which were accurately localized in this series. It has been supposed that the character of the intestinal content at this point, with stasis and chronic mechanical irritation, may account for the increased frequency of carcinoma here. It has been repeatedly pointed out that carcinomas are more malignant in younger than in older persons. Although pathological details are lacking in many of the cases reviewed, there was found to be a high incidence of the tumor type referred to as "colloid," "mucinous," or "gelatinous." Of 73 cases in which the pathological type was indicated, 32 (43%) were of this variety. In contrast, colloid carcinomas make up less than 5% of colon carcinomas in adults. The prognosis of carcinoma of the colon in children is very poor. No cures have been confirmed in patients treated before the age of 16 years, the longest survival being in a girl reported by Webster, who died of a cerebellar metastasis 4 years after her initial treatment.

It has been stated that when cancer of the colon is encountered before the 4th decade of life it is usually on the basis of multiple polyposis or of ulcerative colitis, but none of these 88 cases of carcinoma of the colon seemed to be associated with multiple polyposis. Although it is generally recognized that a significant proportion of patients with untreated familial polyposis will develop carcinoma before the age of 40, it is apparently unusual for the malignancy to become manifest before the age of 20. In only one of the 88 patients was there evidence to indicate the presence of a polyp before the development of carcinoma; this was a 12-year-old boy who gave a history of repeated episodes of cramping lower abdominal pain associated with the passage of bloody mucus since the age of 3 years. The known malignant potential of familial polyposis and of ulcerative colitis and the suspected malignant potential of solitary polyps justify an aggressive therapeutic attitude toward these conditions in childhood. Treatment of carcinoma of the colon in children is essentially the same as in adults; that is, wide block resection to include the primary lesion and the adjacent lymphatic tissue.

A Clinical Comparative Study of Autogenous and Homogenous-Bone Grafts. P. L. Carnesale and J. D. Spankus. J. Bone & Joint Surg. 41A:887-894 (July) 1959 [Boston].

The authors report observations on 143 consecutive bone-grafting procedures in which Merthiolate-preserved, homogenous bone was used, 137 consecutive bone-grafting procedures in which autogenous bone alone was used, and 24 consecutive bone-grafting procedures in which a combination of Merthiolate bank bone and autogenous bone was used. These figures do not include 10 procedures in which there was no follow-up. All bone-grafting procedures done between January, 1948, and January, 1958, are included. The ages of the patients ranged from 19 to 62 years. There were 16 (12%) failures in the autogenous group, 33 (23%) in the homogenous group, and 5 (21%) in the group in which a combination of autogenous and homogenous bone grafts was used. The incidence of failure with autogenous chips was 8%; when a full-thickness autogenous bone block was used, the incidence of failure was 17%. The incidence of failure with homogenous chips was 19%; when a full-thickness block graft was used, the incidence was 31%. A combination of autogenous and homogenous chips resulted in an 18% incidence of failure. The occurrence of infection with Merthiolate-preserved homogenous grafts was less than that with autogenous grafts. Bone grafts inserted in the presence of infection usually resulted in failure. No allergic reaction or sensitivity to Merthiolate occurred, unless one concludes that the greater number of failures from the use of Merthiolate bone is on this basis.

This clinical review confirms the impression that autogenous grafts are superior to homogenous grafts. Homogenous bone grafts are satisfactory in specific situations, but they must be protected for a longer period of time than autogenous grafts. They may be used when the available supply of autogenous bone is not adequate for the particular situation or when the hazard of surgery is materially increased by the obtaining of autogenous bone. Homogenous bone may be used also when no previous plans have been made to obtain autogenous bone. Homogenous bone grafts are often used when a mechanical support is necessary and the condition does not warrant the taking of an autogenous graft; for example, in a depressed plateau fracture of the tibia. The authors believe that they are of the most value in supplementing autogenous bone grafts.

Congenital Muscular Torticollis in Infancy: Some Observations Regarding Treatment. M. B. Coventry and L. E. Harris. J. Bone & Joint Surg. 41A:815-822 (July) 1959 [Boston].

In congenital muscular torticollis a mass appears soon after birth in the belly of the sternocleidomastoid muscle. This is accompanied by a tilt of the head to the side of the muscle involved and by a rotation of the head, so that the chin points to the opposite shoulder. The mass and the tilt and the rotation of the head and neck are accompanied by asymmetry of the skull and facial bones. This asymmetry tends to lessen and, in fact, disappears as time goes on, unless the wryneck becomes a permanent deformity. The pathogenesis of this condition is obscure. It is probably not due to muscle tearing or hemorrhage at birth, and it is, therefore, not a birth injury per se. There is no agreement on a satisfactory treatment of the condition. Available are physical therapy measures, such as stretching and massage, or surgical measures which consist in either section of the sternocleidomastoid muscle, removal of the tumor itself, or a combination of the two.

The authors review observations on 35 infants with congenital neonatal muscular torticollis, who were examined at the Mayo Clinic from 1944 to 1954, inclusive. The infants were born in or near Rochester, Minn. The incidence of congenital muscular torticollis was approximately 0.4%. Nineteen of the patients were girls, and 16 were boys. The sternocleidomastoid tumor was discovered, on the average, 3½ weeks after birth. The tumor disappeared at the average age of 14 weeks. The longest period between time of appearance and time of disappearance of the tumor was 5 months. Facial asymmetry did not usually appear until about 1½ months after the tumor appeared in the sternocleidomastoid muscle. The asymmetry tended to disappear for the most part by the age of 6 months.

Excellent results were obtained in all 24 infants in whom physical therapy (stretching and/or massage) was given, usually by the mother, and in the 6 who were not treated, that is, the patient had no remaining tumor, no apparent deformity of the neck, and no asymmetry of the face or skull. Surgical treatment was employed in the remaining 5 patients. Three of the 5 had excellent results, but 2 had postoperative recurrence of the deformity which required reoperation. The authors do not infer that all patients will get excellent results, without wryneck deformity, if treated nonsurgically. The 2 surgically treated patients who had poor results were operated on at 6 and 19½ months of age, respectively. No immobilizing cast or dressing in the overcorrected position was used. It has been suggested that the overcorrected position should be maintained postoperatively to prevent reattachment of the sectioned muscle and tendon.

The authors conclude that there is no justification for operating on all patients with congenital muscular torticollis in infancy. If there is detectable wryneck deformity with contracture of the sternocleidomastoid muscle after the age of one year, this muscle should be sectioned then because the deformity at that age may be permanent. However, there is every indication that an operation at any age up to 12 years will give as good a result as an operation at an earlier age. The asymmetry of the skull and face will correct itself as long as growth potential is present. The child will grow, and these bones will be reshaped in the absence of the deforming pull of a tight sternocleidomastoid muscle.

Treatment of Giant-Cell Tumor of Bone. E. W. Johnson Jr. and D. C. Dahlin. J. Bone & Joint Surg. 41A:895-904 (July) 1959 [Boston].

This study was undertaken because of conflicting claims concerning the best method of treatment for giant-cell tumors of bone. It is concerned with 116 consecutive cases of giant-cell tumor, taken from the files of the Mayo Clinic. Variants of giant-cell tumor were excluded because of their dissimilarity in regard to response to therapy. By inquiries directed to patients, referring physicians, and relatives, follow-up information was obtained for varying lengths of time on every patient. The ages of the patients ranged from 12 to 71 years, but 63.8% were in the third and fourth decades of life. Women predominated in the ratio of 64 to 52. Sixty-three of the tumors occurred in the upper portion of the tibia or the lower portion of the femur, with the latter site being the most common. The third commonest site was the sacrum, with 11 tumors, and the fourth, the lower portion of the radius, with 9. Since many of these patients received various forms of therapy, either primarily or for recurrences of the tumor, such as excision or amputation after curettage or irradiation, the same patients are considered in more than one treatment category. This has made concise presentation of the results of therapy for each of the 116 patients difficult; yet the results of the various forms of therapy are presented, and the patients are grouped according to the primary treatment given.

In 71 patients curettage was the primary treatment, but it became evident that this is not the ideal treatment, for in 29.6% of the patients treated by this method recurrences developed within the first year after therapy; at the end of 5 years the percentage with recurrences had climbed to 54.1%. Many combinations of treatment were employed for these patients, including curettage with or without grafts, preoperative and postoperative radiation therapy, and chemical cautery of the cavity. None of these ancillary measures appeared to influence the rate of recurrence in this group. A solitary pulmonary metastatic deposit developed in one of the patients 4½ years after the primary lesion in the distal portion of the radius had been controlled by curettage and roentgenotherapy. The primary tumor and the excised metastatic deposit were histologically benign. Amputation became necessary as a secondary procedure in 14 of the patients treated by primary curettage. Secondary sarcoma, massive recurrence, and persistent draining and disabling lesions were the reasons for amputation.

Radiation therapy alone was not successful in controlling any of the giant-cell tumors. There was also no evidence that it diminished the chance of recurrence when used as an ancillary measure with curettage, since the recurrence rate of tumors treated by curettage alone and by curettage combined with radiation was the same. The experience of these authors and of others indicates that radiation therapy may be influential in the genesis of sarcoma secondary to giant-cell tumor. It should be employed only for giant-cell tumors so situated that adequate surgical treatment is impossible.

The tumors of 14 patients were treated primarily by excision, and those of another 4 were completely excised after failure of curettage and ancillary measures. Twelve of the 14 patients had no recurrence while being followed for an average of 16.2 years. Two had unsuccessful results. In one of these, excision of a tumor in the upper portion of the femur was probably successful, but ancillary radiation therapy was given, and the functional result was compromised by radiation necrosis of the acetabulum. The other patient had nonunion after excision of a tumor of the upper end of the tibia, and secondary amputation was necessary. None of the 4 tumors excised after unsuccessful prior therapy has recurred. Tumors for which complete excision, along with removal of all surrounding shells of bone and fibrous tissue, was attempted are an important group from the standpoint of successful treatment. If the giant-cell tumors situated in the sacrum, spinal column, ilium, lower part of the tibia, and the skull are excluded, 79% of those in the series—that is, 92 tumors—could have been excised. To be sure, this implies an aggressive attitude in respect to surgery and a willingness to replace the removed bone with a bone graft or a prosthesis. Early excision, when the lesion is small, involves less loss of bone and easier replacement, whether by graft or prosthesis, than excision used as a secondary form of treatment. Excision is the one successful treatment for these tumors.

Results of Treatment of Congenital Dislocation of the Hip. I. V. Ponseti and E. R. Frigerio. J. Bone & Joint Surg. 41A:823-846 (July) 1959 [Boston].

Beginning in 1942, changes were introduced in the treatment of congenital dislocation of the hip at the State University of Iowa college of medicine in Iowa City. The period of immobilization in a plaster cast was reduced to a maximum of 5 months—usually 3 months in the first position and 6 weeks or 2 months in the second position. This was followed by prolonged functional after-treatment, controlled with an abduction bar or an abduction brace. At county medical society meetings the general practitioners, pediatricians, and obstetricians were instructed in recognition of early clinical signs of this disorder. Early diagnosis made treatment possible in the first years of life and often in early infancy.

The cases of congenital dislocation of the hip were classified in 3 groups: preluxations, subluxations, and dislocations. Hip preluxations were seen in infants under 8 months of age and were characterized clinically by the snapping sign. The displaced femoral head snapped into the center of the acetabulum by pressing the greater trochanter forward and abducting the thighs. In the roentgenograms the upper part of the femur appeared displaced upward or laterally.

In the group of hip subluxations were included children, over 6 months of age, with a limited range of hip abduction, but with a negative snapping sign. In the roentgenograms the small center of ossification of the femoral head appeared to rest under and lateral to the outer edge of the ossified portion of the sloping acetabular roof. This deformity appeared to be more severe than the preluxation and could only be reduced after muscle relaxation, achieved with either general anesthesia or the application of an abduction brace or cast for several days or weeks.

The femoral head was shown to be above the margin of the ossified portion of the acetabular roof in the roentgenograms of patients with conditions classified as dislocations. Hip abduction was often severely limited, but the snapping sign was negative. General anesthesia was required for the reduction of this advanced deformity. During the first year of life no clear line of demarcation exists between preluxations and subluxations. Likewise, during the second and third years the distinction between severe subluxations and low dislocations may be difficult.

The anatomic results of treatment, from 1942 to 1950, of patients under 4 years old with congenital dislocation of the hip and of those with preluxation treated from 1942 to 1954 have been reviewed. Thirty-two patients with 39 hip preluxations with a minimal follow-up of 4 years, 6 patients with 7 subluxations, and 58 patients with 74 hip dislocations and 4 subluxations with a minimal follow-up of 8 years were included in the study. The dislocations were reduced with the child under general anesthesia; only 3 open reductions were done when closed reduction failed. Rotation osteotomy was done on 13 patients. Good anatomic results were obtained in all cases of preluxation and subluxation (groups 1 and 2). Good anatomic results were also obtained in 52 of the dislocated hips; a dysplastic hip resulted in 11 instances. Thus, the femoral head was in a correct position in the acetabulum in 63 of the 74 dislocated hips. Moderate subluxation developed in 5 hips, and severe subluxation in 6. No redislocation occurred.

Closed reduction, followed by carefully supervised treatment, offers satisfactory results in the majority of congenital dislocations of the hip if a child is seen before he is 4 years of age. The importance of early treatment is apparent when the cases are divided into 3 groups. Good anatomic results were obtained in (*a*) all patients initially treated before the age of 1 year; (*b*) 78% of patients who were 1 to 2 years of age; and (*c*) only 57% of those who were 2 to 4 years of age. Early treatment offers the only possibility of obtaining good results almost regularly.

Early Surgical Treatment of Aneurysms of the Circle of Willis. J. L. Pool, J. Ransohoff, M. D. Yahr and J. F. Hammill. Neurology 9:478-486 (July) 1959 [Minneapolis].

The authors do not agree with those who consider surgical intervention of little benefit in the immediate postrupture period in patients with aneurysms of the circle of Willis, but advise major therapeutic efforts during this phase. This report concerns 46 patients who had intracranial clipping of an aneurysm in the so-called early danger period after rupture. Eleven of these patients, however, were either comatose, moribund, or over 55 years of age; the results were so unsatisfactory after early operation that the authors now avoid intracranial operation for most patients in these categories. Therapy must be chosen with regard to the age and neurological and physical condition of the patients and to the location of their aneurysms. Patients who are suspected of having ruptured intracranial aneurysms should be subjected to arteriography as soon as possible, even if this requires transportation to a center where serial angiography is available. The authors observed no ill-effects from such transfers. In patients under 55 years old, who are not comatose, immediate intracranial clipping of their aneurysms under hypothermic anesthesia is advisable.

Direct obliteration provides the best prospects for the patient's long survival, and the earlier this is done, the less is the risk of fatal recurrent hemorrhage, permanent hemiplegia and other neurological deficits, or fatal cerebral edema. Evidence suggests that cerebral vasospasm—and not hematoma—is often responsible for the above complications. The effects of cerebral vasospasm may not become apparent—in the form of hemiplegia, for example—until the 6th to 8th day after aneurysmal rupture. It is advisable to operate prior to the 6th day after hemorrhage, whenever the condition of the patient and the circulatory situation permit. While carotid ligation in the neck may be effective in aneurysms arising from the internal carotid artery or adjacent posterior communicating arteries, the authors reserve this technique for patients in whom direct intracranial attack is impossible for medical reasons, such as a bleeding tendency, cardiac decompensation, or the like.

Multiple aneurysms do not necessarily represent a contraindication to intracranial surgery as long as angiography and clinical examination establish which lesion is actively bleeding. Severe vasospasm is frequently a clue as to which aneurysm has bled. In the series reported, of 5 patients with multiple aneurysms, 2 have undergone bilateral staged surgery, and a third is about to have contralateral craniotomy. A 4th patient has refused reoperation or angiography, despite recent signs pointing to enlargement of her contralateral aneurysm 5 years after initial surgery; her present course indicates the need for treating multiple aneurysms whenever feasible. The 5th patient has 7 aneurysms for which further operation is virtually impossible.

The authors believe, on the basis of having been able to return 27 of a selected group of 35 patients back to full normal activity, relieved of the threat of recurrent bleeding, that many lives can be saved and permanent neurological deficits averted by prompt intracranial attack on aneurysms of the circle of Willis. It also appears that more lives can be saved by operation within the 2-month critical period than by conservative therapy in selected patients.

Open Heart Surgery for Acquired Mitral Insufficiency. F. H. Ellis Jr., R. O. Brandenburg, J. A. Callahan and H. W. Marshall. A. M. A. Arch. Surg. 79:222-237 (Aug.) 1959 [Chicago].

The authors report on 8 men and 7 women, between the ages of 23 and 52 years, who were operated on for acquired mitral insufficiency at the Mayo Clinic. Most of the 15 patients had relatively pure mitral insufficiency; 2 also had moderate mitral stenosis; and 5 had ruptured chordae tendineae. The tissue of the posterior leaflet was deficient in 10. The mitral ring was dilated in 9. A bilateral, anterior thoracotomy incision through the bed of the nonresected 5th rib was used in 5 patients. Although this incision gives excellent exposure, the authors prefer an anterolateral incision through the bed of the nonresected 5th or 6th rib, and this right lateral approach without induction of cardiac arrest was used in 10 patients. A variety of surgical techniques was employed, including mitral annuloplasty, plication of the elongated leaflet with ruptured chordae tendineae, and use of a compressed roll of Ivalon as a substitute for deficient posterior leaflet tissue. There were 3 hospital deaths, and one patient died suddenly in heart failure 2 months after the operation. Of the 11 surviving patients, 8 were followed up long enough for evaluation, i. e., for from 3 to 12 months, and 7 of these obtained excellent functional results and 1 was improved. The hemodynamic findings in 9 patients studied by right heart catheterization soon after the operation showed in all the patients normal or near normal values of all physiological variables studied. Of 3 patients studied after an additional interval of several months, 2 showed evidence of some recurrence of mitral insufficiency.

Further time must elapse before this approach to the correction of acquired mitral insufficiency can be fully evaluated. At present the authors are advising open-heart repair for patients with relatively pure mitral insufficiency when significant progressive functional disability is present.

Surgical Therapy of Mitral Stenosis in Pregnancy: 26 Personal Observations. A. Actis Dato, R. Gentilli, V. Levi and others. Minerva med. 50:1905-1918 (June 13) 1959 (In Italian) [Turin, Italy].

Twenty-six pregnant women, aged between 22 and 41 years, with mitral stenosis underwent mitral commissurotomy between the 3rd and the 6th month of pregnancy. Sixteen patients had been previously pregnant and had term delivery; 4 had had either therapeutic abortion alone or therapeutic abortion and term delivery; and 6 had never been previously pregnant. Pure mitral stenosis had been established on auscultation in 14 patients. Sinus rhythm, which in some instances was accompanied by a slight tachycardia or bradycardia, was observed in 24 patients on electrocardiographic examination. The size of the mitral orifice at operation was found to be very small in most patients, ranging from 0.4 to 1 sq. cm.

After the operation, patients had a moderate chest pain related to the operative trauma; pleural effusion took place in 18 patients, and moderate dyspnea in a few. The body temperature was normalized within 7 days after the operation. Atrial fibrillation, which developed in 3 patients who had preoperatively had sinus rhythm, subsided with a cardiokinetic treatment within a few days. Digitalis was given to the patients in the immediate and the later postoperative period. No patient died either during or after the operation. Intrauterine death took place in 1 instance, and spontaneous abortion in 2. A patient underwent successful cesarean section at term. The postoperative course was very good in 21 patients, good in 3, and fair in 2. No postoperative rheumatic episodes developed. The authors believe that evaluation of a surgical correction of mitral stenosis in pregnancy should be made with the same criteria as in instances in which there is no pregnancy. Surgical correction of mitral stenosis is indicated during the first period of pregnancy, provided that either pure mitral stenosis or conditions in which mitral stenosis is the main disorder are present. No therapeutic abortion is necessary.

Solitary Pulmonary Nodule. G. H. C. Joynt and K. P. Vassal. Canad. M. A. J. 81:78-81 (July 15) 1959 [Toronto].

Sixty consecutive resections of solitary pulmonary nodules, performed over a 10-year period (1948-1959), are reported. The patients were 28 to 72 years of age. Twenty-eight patients presented a malignant tumor of the lung; 10 were treated by pneumonectomy, 17 by lobectomy, and 1 by segmental resection. The pathological reports in these 28 patients showed 10 anaplastic or undifferentiated tumors, 8 epidermoid or squamous-cell carcinomas, 8 adenocarcinomas, and 2 alveolar (cell) carcinomas. Most of these patients were male; there were 9 females, 4 of whom presented adenocarcinoma and 2 alveolar (cell) carcinoma. Eleven resections were carried out for primary carcinoma of the lung between 1948 and 1953; the 5-year follow-up revealed that 6 of these patients had died, 3 could not be traced, and 2 (one with an adenocarcinoma and the other with a squamous-cell carcinoma) were alive and well. Of the 28 patients with primary lung carcinoma, 10 died within 2 years; the greatest mortality occurred within the first year after the operation. A high proportion of anaplastic carcinomas was found among the 28 patients.

There was no definite proved lesion caused by a fungus in 22 granulomas observed in the total series. Cultures for tubercle bacilli and guinea-pig inoculation were carried out in 13 patients; a positive result was obtained in 6. Two of the 6 patients were sent to a sanatorium for postoperative management with antimicrobial drugs, one being treated for a year and then returned to work, the other being treated for 6 months. The remaining 4 patients returned to work 2 or 3 months after the operation, but they were treated with antimicrobial drugs for 6 months postoperatively. Three of 5 metastatic tumors present in the series originated from a hypernephroma, one from an osteogenic sarcoma, and one from a melanotic sarcoma. The patient with the latter is still alive and well 3 years after pulmonary resection. One patient with a metastatic lesion from a hypernephroma is also living. The patient with the metastatic tumor from the osteogenic sarcoma died 3 years after the operation.

All 60 patients survived the operation, and no serious complications were encountered. The morbidity was minimal, and frequently the patient returned to work in 2 or 3 weeks. A more conservative approach was adopted when the pulmonary nodule was frankly caseous and contained tubercle bacilli. The authors believe that, with few exceptions, isolated intrapulmonary nodules are best treated by prompt surgical exploration, unless an exact preoperative diagnosis is possible or a malignant tumor can be excluded with certainty.

Thoracic Esophageal Diverticula: Report of Three Cases. T. W. Shields and M. C. Anderson. Am. J. Digest. Dis. 4:522-533 (July) 1959 [New York].

Intrathoracic esophageal diverticula may be considered either epibronchial or epiphrenic according to their point of origin in the intrathoracic esophagus. The mechanisms of pathogenesis are considered to be a combination of traction and pulsion as well as neuromuscular incoordination. The traction diverticulum consists of all coats of the esophageal wall and arises from external pull exerted by various extrinsic lesions on the wall of the esophagus. The pulsion diverticulum consists of the mucosa, the lamina propria, and at times the circular muscular layer which herniates through a defect in the longitudinal muscular wall of the esophagus. The traction-pulsion diverticulum arises and persists as a result of both intrinsic and extrinsic factors, and undoubtedly such a mechanism is common to many of the intrathoracic diverticula. The functional diverticulum, transient in nature, is an apparent diverticulum arising from incoordination of esophageal muscular activity. An epibronchial diverticulum arises in the region of, or above, the tracheal bifurcation, and an epiphrenic diverticulum in the distal segment of the esophagus just above the diaphragm. The diagnosis of an epiphrenic diverticulum depends on roentgenographic examination of the esophagus with barium or other contrast mediums. Once a diverticulum has been demonstrated roentgenographically, other lesions must be ruled out as the source of symptoms. Studies of the stomach, duodenum, and biliary tract, as well as electrocardiograms, are essential.

Patients with epibronchial diverticula should be treated surgically to prevent complications. Complications of epiphrenic pouches are infrequent, but, as with epibronchial diverticula, infection and ulceration may occur. Hemorrhage or perforation, with subsequent mediastinitis, empyema, or bronchopleural fistula, may be the result of these. Esophageal stricture or carcinoma has occasionally been associated with an epiphrenic diverticulum, as well as pulmonary infection from regurgitation and aspiration or as a direct result of fistula formation. The histories of 3 patients in whom epiphrenic diverticula were discovered incidentally by roentgenographic examination of the esophagus with barium are presented. Transthoracic excision of the diverticula relieved the patients of their complaints.

Aortic-Pedicle Technic for Obtaining Immediate Vascularization of Fetal Parathyroid-Gland Transplants in Man: Application in Three Patients with Hypoparathyroidism Appearing After Thyroidectomy. E. Watkins Jr., L. L. Haynes and H. D. Adams. New England J. Med. 261:105-112 (July 16) 1959 [Boston].

Since medical management of chronic deprivation of parathyroid function as a result of operation may give rise to renal or ophthalmic complications over a period of years, it would be desirable to provide an endogenous source of parathyroid secretion by transplantation of functioning gland into the patient. A variety of methods have been used for the homologous transplantation of parathyroid glands. Fragments of the endocrine tissue have been grafted without immediate reestablishment of blood vessel continuity. Some of these transplants appear to have been tolerated despite genetic dissimilarity between donor and host. A grafting method should meet 2 additional criteria: the parathyroid gland should be derived from a newborn infant—preferably a premature infant—within a short time after birth; and the embryonic gland should be connected to the host by surgical anastomosis of blood vessels. The first requirement is based upon the evidence that embryonic endocrine tissue is less likely to evoke an immune reaction than adult tissue, and the second criterion assures immediate nutrition of the parathyroid homograft.

Transplantation of a vascularized pedicle of pretracheal tissue from a premature infant affords a method of transplanting minute parathyroid gland tissue from an immature neonate into a patient with parathyroid deficiency. All pretracheal tissue encompassing the minute thyroid and parathyroid anlage is removed in continuity with the aorta and superior vena cava. These larger vessels are anastomosed to suitable vessels in the groin of the deficient patient, and channel blood to the tissues of the pedicle. The method affords adequate vessels for surgical anastomosis despite the small size of the fetal parathyroid gland. Evidence indicates that embryonic tissue survives homologous transplantation more readily than adult tissue. The method described assures adequate immediate blood supply to such embryonic tissue. The aortic-pedicle technique may be useful in transplantation of other embryonic endocrine tissues.

The method has been applied in 3 patients suffering from chronic hypocalcemic tetany after thyroidectomy. In the first patient, grafting early in 1956 was followed by the complete elimination of all medication requirements and striking improvement in the patient's mineral equilibrium, nutrition, sense of well-being, and ability to perform strong muscular exercise; in this case tetany was relieved. In 2 additional patients recently subjected to the grafting procedure, tetany persists, but the interval elapsing is too short to permit conclusions concerning the status of the transplant.

Biopsy Technique in the Diagnosis of Intrathoracic Disease. B. R. Lawton. Wisconsin M. J. 58:351-355 (July) 1959 [Madison].

The development of specific therapy for increasing numbers of intrathoracic diseases has made mandatory the establishment of histopathological or microbiological diagnosis in every case possible. This prompted the author to present his experience with little used biopsy techniques carried out in 60 patients. The total of 75 biopsy procedures comprised 54 scalene node biopsies, 13 pulmonary biopsies, and 8 pleural biopsies. Positive diagnosis was established by biopsy in 33 patients, or 55% of those in this series. In the remaining 27 patients, a diagnosis was established later by thoracotomy in 13 and at autopsy in one; in 13 patients microscopic diagnosis was not established.

In an attempt to better establish the indications for these procedures, the author tried to correlate positive biopsies with specific x-ray findings. It was found that, in 19 cases in which the radiologist described enlarged hilar nodes, 6 had positive scalene node biopsies. Of 21 cases showing diffuse pulmonary infiltration, scalene nodes were abnormal in only 5, and 2 of these were not diagnostic. This reduces the diagnostic usefulness to 14% in this type of case. Therefore, scalene node biopsy in cases of diffuse pulmonary infiltration has been abandoned in favor of primary pulmonary biopsy. To illustrate the usefulness of biopsy procedures, paired x-rays are presented which show that, in each pair of cases with similar x-ray findings, the diagnoses are totally different and treatment diametrically opposed. With more liberal and logical application of these techniques, further improvement is anticipated.

Controlled Blood Pressure Reduction and Artificial Hypothermia as Emergency Measure in Threatening Hemorrhages from Esophageal Varices. G. Kuhlgatz. Chirurg 30:296-299 (July) 1959 (In German) [Berlin].

Transfusion of whole blood and the administration of oxygen are the most important emergency measures in patients with acute bleeding from esophageal varices. In some patients it is advisable to introduce the blood intra-arterially under pressure by way of the femoral artery. Even this procedure, in some instances, fails to control the circulatory collapse, because the hemorrhage may increase as the blood pressure rises parallel to the refilling of the depleted circulation, or an arrested hemorrhage may commence again. Under these conditions, determined efforts have to be made to arrest the hemorrhage by conservative means until the patient's general condition permits a surgical intervention.

In 6 patients with massive hemorrhages from esophageal varices, in whom other conservative measures had failed, the author succeeded in arresting the hemorrhage by controlled blood pressure reduction in combination with artificial hypothermia. In 4 of these patients bleeding did not recur, even after the blood pressure had been normalized; this permitted adequate preparation for the surgical treatment, which had been inadvisable because of the poor general condition (cirrhosis of the liver, jaundice, ascites). In the remaining 2 patients the hypotension permitted the refilling and stabilization of the circulation, so that the operations could be carried out under favorable conditions—in one patient resection of the cardia with esophagogastrostomy, and in the other transthoracic ligature of the varices.

The case histories of the 6 patients show that blood pressure reduction was produced with the aid of adrenergic blocking agents, such as Hydergine, and by ganglionic blocking agents, such as hexamethonium, also by putting the patients in a suitable position. Artificial hypothermia was induced with the aid of ice packs, until the rectal temperature had been reduced to as low as 26 C (78.8 F) in one of the patients, but in the others to only 28 to 34 C (82.4 to 93.2 F). Hypothermia was usually continued for 2 days, and hypotension for several days longer. The author advises against artificial reheating by means of heat packs and short-wave treatment, and prefers to await spontaneous restoration of normal body temperature. He emphasizes that the use of hypotension plus hypothermia requires high standards of nursing care: frequent changing of the patient's position, because of the greater predisposition to decubitus ulcers, also cleansing enemas, bladder irrigations, feeding by nasal tube, and continuous control of circulation, respiration, temperature, and fluid and mineral balance.

Supra- and Transduodenal Exploration of the Common Bile Duct. H. Mahorner. Am. J. Gastroenterol. 32:182-189 (Aug.) 1959 [New York].

A series of 445 operations for benign lesions of the biliary tract have been analyzed and used as a basic study. There are several advantages in the transduodenal approach when exploring the common bile duct: soft tissue obstruction may be visualized; pancreatitis and stenosis of the ampulla, a true organic obstruction, may be obviated by ampullotomy; and carcinoma of the ampulla of Vater may be discovered, and a proper operation (pancreatoduodenectomy) may be performed. Carcinoma of the pancreas, easily overlooked otherwise, was found twice in this series of 445 operations for benign lesions. One of the patients was cured by pancreatoduodenectomy; the carcinoma of the other, which had been overlooked 3 times elsewhere during common bile duct exploration, recurred after local removal. Three times in this series of duct exploration, stones were known to have been left; this occurred when the supraduodenal approach alone was used. A higher percentage of stones were removed when the combined supraduodenal and transduodenal approach was used (50%) than when the supraduodenal route alone was employed (27%).

Opening of the common bile duct is indicated in case of obstruction, either from stones or from soft tissue, such as pancreatitis or ampullitis, or from carcinoma at the end of the duct, but it is definitely contraindicated when there is no obstruction. The opening of the common duct is justifiable in patients with jaundice or with a history of jaundice. When stones were recovered from the common bile duct in patients of this series, jaundice was present in approximately 54% of the patients, and was absent in 46%. This clearly demonstrates that the absence of jaundice does not exclude the presence of stones in the common bile duct. The evidence at operation was found to substantiate the diagnosis of pancreatitis in 25 of the patients. In 24 of these the common duct was explored, and in 1 a decompression was obtained by cholecystostomy. All the patients recovered.

A comparison of the results obtained by the supraduodenal approach, performed on one-half of the patients, with those obtained by the combined supraduodenal and transduodenal method, used in the other half, showed that mortality was not higher in the group in which the combined method was used. This, however, does not mean that the combined method is safer; it must, in fact, be used judiciously and with technical precision. The indications for opening the duodenum after having made a supraduodenal opening in the common bile duct are as follows: (1) presence of multiple stones in the common bile duct, in case their complete removal or the free passage of the sound into the duodenum is doubtful; (2) presence of pancreatitis; and (3) uncertainty as to whether the sound has passed into the duodenum. The contraindications for opening the duodenum are as important as the indications, and are as follows: (1) massive edema of the gastrohepatic omentum and the duodenum, such as is frequently found with acute cholecystitis; (2) acute hemorrhagic pancreatitis; (3) debilitated condition of the patient; and (4) age of elderly patients, unless a stone is known to be impacted in the ampulla of Vater necessitating this operation. It is advisable to perform a two-stage operation in patients with acute cholecystitis associated with edema, performing cholecystostomy first and leaving exploration of the common bile duct until later. Even when justifiable indications exist for exploring the common bile duct, the contraindications may be stronger under certain circumstances of acute infection, when clear identification is not feasible without accepting exceptional hazard.

The Kidneys in Surgery of the Abdominal Aorta. D. E. Szilagyi, R. F. Smith and J. G. Whitcomb. A. M. A. Arch. Surg. 79:252-268 (Aug.) 1959 [Chicago].

The authors report on 250 patients, most of them men, between the ages of 50 and 65 years, with arteriosclerotic disease of the abdominal aorta for which they were operated on at the Henry Ford Hospital in Detroit. Observations on these patients showed that it is not only prudent but physiologically correct to regard every patient with arteriosclerotic disease of the abdominal aorta severe enough to require surgical treatment as having a reduced renal reserve and, therefore, a diminished ability to withstand the physiological assault of an operation of great magnitude. Aside from the elusive injuries of operative trauma, the kidneys may be subjected to direct physical damage in 2 ways peculiar to aortic surgery: through ischemia due to occlusion of the abdominal aorta by clamping, and through chemical trauma inflicted through the injection of contrast mediums in the course of diagnostic studies.

Although cross clamping of the abdominal aorta distal to the renal arteries has not been found responsible for any specific physiological injury, its harmful potentialities must be kept in mind. The safe period of cross clamping of the aorta above the renal arteries has been found to be 30 minutes for kidneys without manifest organic disease. In operative procedures requiring longer clamping, renal circulation must be maintained by some form of bypass. Nine (18%) of 50 patients from whom aortograms were obtained with the aid of 70% sodium acetrizoate (Urokon) showed significant depression of renal function for 48 hours to 11 days after the aortography. The use of the least toxic contrast medium (diatrizoate [Hypaque] sodium), in the smallest possible amount, with multiple exposure technique for the avoidance of repetition of injection, is recommended. The usefulness of the determination of the preaortographic and the postaortographic serum creatinine level as a functional index of renal function is stressed.

The possibility of the presence of accessory renal arteries must be remembered in the course of operative dissection of the abdominal aorta. Whenever the aortic dissection reaches above the level of the inferior mesenteric artery, the left renal vein must be looked for, and, if it is not found in its normal anatomic location, it must be sought in a retroaortic position. In dealing with horseshoe kidneys associated with an aneurysm of the abdominal aorta, bisection of the renal isthmus, suture of the cut ends, and resection of the separated kidneys allow the removal of the aneurysm in the routine manner. When an abdominal aneurysm is complicated by ureteral obstruction, the resection of the aneurysm is indicated at the earliest safe moment.

Pseudomembranous Enterocolitis: The Experimental Induction of the Disease with Staphylococcus Aureus and Its Enterotoxin. J. V. Prohaska. A. M. A. Arch. Surg. 79:197-206 (Aug.) 1959 [Chicago].

In an attempt to correct existing misconceptions concerning the pathogenesis of pseudomembranous enterocolitis, and prompted by the fact that this disease persists as a serious and often fatal complication of major surgical procedures, the author performed experiments on chinchillas, cats, and kittens. Fatal enterocolitis was induced in chinchillas to which particular strains of staphylococci had been administered orally after the animals had been given an antibiotic mixture consisting of 12.5 mg. of chlortetracycline (Aureomycin), 12.5 mg. of oxytetracycline (Terramycin), and 25 mg. of sulfisoxazole (Gantrisin). Fatal enterocolitis was also induced by the oral administration of staphylococcic enterotoxin to chinchillas which had never received antibiotics. Nonfatal enteritis was induced by the oral administration of staphylococcic enterotoxin to cats and kittens which had likewise never received antibiotics.

The enterotoxin given to these animals was extracted from cultures of staphylococci which represented pure isolates from stools of patients seriously ill with pseudomembranous enterocolitis or from a culture of staphylococci isolated from frozen shrimps known to be implicated in food poisoning. The stool cultures of the experimental animals remained normal, and at autopsy no staphylococci could be isolated. The absence of staphylococci in the intestinal tract of the animals receiving only the enterotoxin indicates that the enteritis is produced by the enterotoxin alone. It is concluded that pseudomembranous enterocolitis develops in man when colonies of staphylococci are able to grow in his intestine and elaborate enterotoxin. The symptoms of pseudomembranous enterocolitis, the physical changes observed in the intestine, and the fatal termination of the disease are due to the enterotoxin.

Results of Subtotal Gastrectomy in 449 Patients with Benign Peptic Ulcer. R. M. Penick and R. A. Armstrong. Am. J. Gastroenterol. 32:152-157 (Aug.) 1959 [New York].

The results of subtotal gastrectomy performed during the years from 1942 through 1956 at the Ochsner Clinic, in New Orleans, were evaluated. A total of 462 patients were operated on for benign peptic ulcer of the duodenum or stomach; included were 314 patients with duodenal ulcer, 123 with gastric ulcer, and 25 with gastrojejunal ulcer. Of these, 449 were subjected to subtotal gastrectomy. Adequate follow-up data were obtained in 413 patients. The operation consisted of a posterior Hofmeister modification of Billroth II, with removal of 75% of the stomach or more. The total postoperative mortality rate in patients in whom conservative resection was made was 1.8%, which was slightly higher when 80% or more of the stomach was removed. On the other hand, gastrojejunal ulcer as a sequela to gastrectomy developed in only 1.3% of the patients in whom radical operation was performed, as compared with the occurrence of this complication in 10% of those who were subjected to conservative resection. These statistics substantiate the belief that the incidence of this complication is in direct relation to the amount of stomach removed. Thus, satisfactory results were obtained in 90% of the patients. Subtotal gastrectomy, when correctly performed, has proved to be a satisfactory operation in the authors' experience, despite the fact that the patients in this series were a selected group with a high tendency to peptic ulceration.

NEUROLOGY & PSYCHIATRY

Effect of Lidocaine Intravenously on Epileptic Attacks. E. Bohm. Nord. med. 61:885-889 (June 11) 1959 (In Swedish) [Stockholm].

The effect of intravenous injections of lidocaine on epileptic seizures, mainly grand mal and jacksonian attacks, was studied in 52 patients in the neurosurgical clinic of the Serafimer Hospital. The diagnosis on admission was cerebral tumor in 27 cases, epilepsy in 18, acute encephalitis in 1, and acute brain damage in 6. Lidocaine was administered either in a single dose or continuously in intravenous drip infusion of saline or dextrose solution. Eleven of 12 grand mal attacks in 7 patients were arrested with a single dose of lidocaine of from 0.5 to 3 mg. per kilogram of body weight. In 15 attacks of status epilepticus of grand mal type in 12 patients, the agent was given in doses of between 2 and 10 mg. per kilogram of body weight per hour. Full effect was seen in 7 patients after the administration of from 4 to 6 mg. of lidocaine per kilogram of body weight per hour. In 2 patients given 8 mg. per kilogram, the attacks occurred in the early postoperative course after extirpation of a brain tumor, and the effect was only partial; both patients had postoperative hematomas. Since lidocaine in the doses given has no narcotic effect, the probable diagnosis of postoperative hematoma could be made and verified. This was also the case in a patient given 10 mg. of lidocaine per kilogram of body weight per hour where reoperation revealed cerebral edema with malacic brain tissue in the operation area. In 36 jacksonian attacks in 27 patients, lidocaine administered intravenously in doses of from 1 to 10 mg. per kilogram of body weight was beneficial in 23 patients. In 23 attacks of status epilepticus of jacksonian type in 21 patients, lidocaine was administered continuously in doses of from 1 to 10 mg. per kilogram of body weight per hour; in 14 cases a blocking effect resulted with doses between 6 and 8 mg. In some cases of myoclonic epilepsy and continuing local motor seizures, lidocaine had no effect on the convulsions.

Migraine Plus Epilepsy. W. C. Alvarez. Neurology 9:487-491 (July) 1959 [Minneapolis].

The author presents case histories which indicate that, when one has to deal with a person with unusually severe migraine or migraine still severe in the person's later years, one should think of a second component, which sometimes is epilepsy or an epileptic carrier state. The author gives several reasons for his inability to accept the thesis that migraine is closely related to epilepsy. It seems more probable to him that, when epilepsy and migraine are found together in a patient, they are due to 2 inheritances.

Persons with simple or typical or mild migraine seldom have epileptic relatives, but in a study made by the author, 21% of 99 relatives of epileptics had had migraine. This does not prove a relationship between the 2 diseases, because, in a group of 574 relatives of psychotic or alcoholic persons, 23% were found to have migraine, and migraine and psychosis do not appear to be at all related. Persons with pure migraine have normal electroencephalograms, and they are not helped by anticonvulsive drugs. Persons suffering from migraine are usually very different—physically, intellectually, socially, and temperamentally—from persons suffering from epilepsy.

A series of cases are described in which persons with a severe form of migraine had either what looked like an epileptic inheritance or actual epilepsy in themselves. It is well to recognize epilepsy when it is added to migraine, because epilepsy can explain so easily the severity of the syndrome and occasionally can lead to a cure with the help of anticonvulsive medication. A few epileptic patients will be found to have mild migraine.

The Significance of Complement-Fixing and Neutralizing Antibodies for the Diagnosis of Infections with the Virus of Lymphocytic Choriomeningitis. W. Scheid, R. Ackermann and K.-A. Jochheim. Deutsche med. Wchnschr. 84:1293-1296 (July 17) 1959 (In German) [Stuttgart, Germany].

The virus of lymphocytic choriomeningitis (LCM), which was isolated for the first time in the United States in 1934, elicits different clinical entities. It is not definitely known whether the syndrome of abacterial meningitis is a particularly frequent clinical manifestation of this virus. In addition to meningitides that take a favorable course, the LCM virus is known to produce fatal encephalitides as well as acute encephalomyelitides. Mild febrile infections without any neurological symptoms may also be caused by the LCM virus, but since they will be traced to the virus only in rare cases, the incidence of infections with this virus is difficult to estimate. Since the LCM virus is usually transmitted to humans by house mice, extensive epidemics need not be feared. Sporadic as well as endemic infections with the LCM virus occur in Germany, but because they produce varied clinical pictures, only laboratory tests will establish the connection between the disorder and the virus. In the rapidly fatal cases, the isolation and identification of the virus will have to suffice for the verification of the diagnosis. In other cases, however, serologic studies are required.

The authors present the results of tests in 15 patients to show that complement-fixing antibodies may appear already during the first week of the infection, although in most instances they appear later. High titer values are usually obtained from the 3rd to the 6th week. While in one instance complement-fixing antibodies had disappeared by the 5th month, usually they were found to disappear more slowly, sometimes persisting for many months or for several years. The neutralizing antibodies, which the authors were able to demonstrate in all their cases, appeared earlier than had been assumed. Convincing titer values were found already a few weeks after the onset of the illness, but the maximal neutralization titers were not observed until after the third month, and not even after several years could a loss of such antibodies be demonstrated. The behavior of the complement-fixing and neutralizing antibodies permits deductions about the onset of the infection. Obtaining a serum specimen during the first few days of the illness is of great importance for the serologic diagnosis of infections with the LCM virus.

Corticotropin Therapy in Epilepsy (Gibbs' Hypsarrythmia). C. Hansted and F. Thygesen. Nord. med. 61:895-899 (June 11) 1959 (In Danish) [Stockholm].

Gibbs's hypsarrythmia designates a grave electroencephalographic abnormality, characterized by high amplitudes, irregular potentials, and incessantly varying spikes. The abnormality is apparently always accompanied by an infantile epilepsy form. Authors agree that the disorder usually sets in in the first year of life, rarely after the third year. The children have up to 100 spasms a day. Some children die in a few years; most of them end with a grave dementia developed coordinately with the epileptic seizures. Practically no child, under 3 years of age, with clinical grand or petit mal epilepsy presents hypsarrythmia. The predilection of hypsarrythmia for the first years of life may point to a pathogenetic significance of constitutional factors, not necessarily hereditary. Sorel and Dusaucy-Bauloye in 1958 published the results of treatment of 7 children with hypsarrythmia with corticotropin (ACTH); 6 of the children became free from spasms after several days' treatment. The children have been followed for from 2 months to 2 years.

In the case presented here, in a girl, aged 5 months, without familial predisposition to epilepsy or other disease and with normal development, motor epilepsy set in in the course of a few days. For 3 or 4 weeks often more than 100 attacks occurred daily, mostly lasting a few seconds; otherwise no signs of organic disease were seen. Electroencephalographically there were a number of almost continuous disorganized and extremely abnormal curves. The condition was aggravated during phenobarbital treatment and did not improve on dimedione treatment. Administration of corticotropin for 10 days, started a month after the onset of the disorder, was followed by complete remission. No recurrence was seen on ambulant observation for 5 months. If time confirms the corticotropin effect described, the process must be regarded as initially reversible.

Clinical Indications and Toxicity of Prolonged Perphenazine Therapy. F. J. Ayd Jr. New England J. Med. 261:172-174 (July 23) 1959 [Boston].

Clinical experience with tranquilizers in the treatment of chronic neurotic and psychotic disorders has demonstrated that they must be administered for prolonged periods. Questions about possible deleterious effects from long-term use of phenothiazine derivatives, such as perphenazine, induced the author to subject to a complete laboratory survey (consisting of hematological examination, liver-function tests, and urinalysis) 50 patients (36 women and 14 men), who had received perphenazine for disabling anxiety, tension, or psychomotor excitement. None had responded to previous treatment, including other tranquilizers (21 cases), the shock therapies (19), and psychosurgery (3). After 19 to 34 months of therapy (minimum total dose, 3,507 mg., and maximum total dose, 35,445 mg.), all had improved and were ambulatory and functioning effectively. Side-effects (none serious) occurred with initial high dosage, but all disappeared with the establishment of maintenance dose.

The laboratory tests were made before and at repeated intervals during the treatment, also at the end of the survey. The results of the tests were all within the range of normal variation, with the exception of changes in the cephalin flocculation in 4 patients. These changes were not statistically significant. Whether they were due to perphenazine or other circumstances is unknown. On the basis of the laboratory findings in this survey, it appears that the drug had no demonstrable deleterious effect on the blood, liver, or kidneys in these patients. Like other phenothiazine tranquilizers, perphenazine does not cure but effectively controls symptoms with a minimum of autonomic, endocrine, and neurological side-effects. Its chief value lies in the small degree of functional disability that it causes, despite its potency. Its use shortens the hospital stay, accelerates symptomatic remission, and permits ambulatory treatment for many patients over prolonged periods safely.

GYNECOLOGY & OBSTETRICS

The Treatment of Inefficient Uterine Action with the Intravenous Oxytocin Drip: A Review of 300 Cases. L. Goldman. J. Obst. & Gynaec. Brit. Emp. 66:382-393 (June) 1959 [London].

The author reports on 300 parturient women who had not reached half-dilatation after 12 hours of established labor and, therefore, were regarded as cases of inefficient uterine action and were treated by the intravenous oxytocin drip. These women represented less than 2% of the total deliveries on the obstetric wards of the King Edward VIII Hospital and McCord's Zulu Hospital in Durban, Union of South Africa, over the same period. Of the 300 patients, 251 (83.7%) were primiparous—an expected finding because inefficient uterine action is mainly a complication of first labors. However, there were also 7 patients who had had more than 5 deliveries. The solution used for treatment was that of 0.4 cc. (4 units) of Pitocin (a proprietary preparation of oxytocin) in

1,000 cc. of 5% dextrose in water, i. e., a dilution of 1 to 2,500, set up to run at 10 drops a minute. The rate of flow was increased if there was no effective response, but rarely beyond 30 drops a minute. As a result of the treatment, 257 patients reached full-dilatation within 12 hours, a success rate of 85.7%. The perinatal loss, excluding those cases in which intrauterine death of the fetus had taken place before starting the drip, was 31 per mille. Cesarean sections were performed on only 3% of the patients.

Analysis of the 43 therapeutic failures indicated that the duration of cervical stasis was the most important single feature determining a good response to the treatment. High heads, posterior positions, malpresentations, and incoordinate uterine action did not offer any contraindication to the successful and safe use of the drip. A review of the literature on rupture of the uterus associated with intravenous oxytocin drip therapy did not reveal a single case of rupture of the uterus occurring in a primiparous patient. Three cases of rupture of the uterus associated with the use of Pitocin for the induction of labor were reported; all of these occurred in multiparous women. The only valid contraindication to oxytocin drip therapy is the risk of rupture of the uterus in the multiparous patient. It is suggested that a more dilute solution should be employed in multiparous patients, and administration should be extremely cautious. No oxytocic agent should ever be used in a suspect uterus. Inefficient uterine action has been defined in terms of cervical stasis, and a plea is made for a therapeutic trial of oxytocin in all primiparous patients with cervical arrest at 2 or more fingers dilatation for longer than 6 hours.

A Clinical Evaluation of Chlorothiazide in the Prevention and Treatment of Toxemia of Pregnancy. L. J. Salerno, M. L. Stone and P. Ditchik. Obst. & Gynec. 14:188-192 (Aug.) 1959 [New York].

The authors report on 102 pregnant women with varying degrees of pitting edema or toxemia (indicated by edema, hypertension, and proteinuria), who were treated with chlorothiazide (Diuril) in the prenatal clinic of the New York Medical College–Metropolitan Medical Center. Chlorothiazide was administered orally in doses of 500 mg. in the morning and 500 mg. at night, a total of 1,000 mg. daily. The average weight loss during the first week of treatment was 5.16 lb. (2.4 kg.), and at the same time the edema had either completely disappeared or had diminished considerably. Edema persisted in 18 of the 102 patients after one week of therapy. After initial treatment blood pressure remained unchanged in 72 patients, was decreased in 20, and was elevated in 10. After the first week of treatment side-reactions occurred in 25 patients, 9 of whom had nausea, 3 vomiting, 7 dizziness, and 6 drowsiness. In only 4 patients were the symptoms severe enough to discontinue therapy. In those patients in whom the drug was withdrawn after the first 7 days of its administration, a rebound phenomenon was invariably noted; it was observed that most of the patients within a period of one week had regained more than the initial weight loss. When the administration of chlorothiazide was continuous, rebound occurred much less frequently and was less marked.

Seventy-one patients were observed during 2 or more weeks of treatment with chlorothiazide; of these, 40 were treated for 4 to 18 weeks, some intermittently and many continuously, with 1,000 mg. of the drug given daily. In the longest continuous therapy, 1,000 mg. of chlorothiazide was administered daily for 17 weeks. Continuous or prolonged therapy maintained good control of edema and weight gain in 62 of the 71 patients. Of the 24 patients with toxemia of pregnancy, the conditions of 11 were improved, 2 remained unchanged, and 11 showed worsening of the toxemic state. There were no demonstrable specific hypotensive effects of chlorothiazide given alone, and no observable potentiation of other hypotensive agents. Chlorothiazide is to be considered an ideal diuretic in the treatment of edema of pregnancy and in the prevention and control of toxemia of pregnancy. Side-reactions are few and minor in nature, and there are apparently no harmful effects of prolonged and continuous administration of the drug. Any specific hypotensive effect cannot be ascribed to chlorothiazide.

PEDIATRICS

Aspects of Hyaline Membrane Disease in Premature Infants. S. Friedrich. Ztschr. Kinderh. 82:357-386 (no. 4) 1959 (In German) [Berlin].

This report is based on the author's observations on 40 premature infants, and on the histories of 103 premature infants who died in the neonatal period. For statistical evaluation, records were kept for all the newborn premature infants who were hospitalized between February, 1956, and February, 1957, at the Children's Hospital in Leipzig, Germany. Hyaline membrane disease was found predominantly in infants who died during the first 3 days of life, and who weighed between 1,000 and 2,000 Gm. (2.2 and 4.4 lb.). Signs and symptoms suggestive of hyaline membrane disease were respiratory distress (retraction expiratory grunt, alae nasi movements, increased rate of breathing, dyspnea), grayish pale cyanosis, and restlessness. Diagnosis was also based on the course of the disease, its severity not being evident at birth but appearing soon after.

The clinical aspects of hyaline membrane disease can be distinguished (*a*) from aspiration of the amniotic fluid and atelectasis by the inconspicuous symptoms in the immediate postnatal period, then by the gradual increase in respiratory activity, a marked progressive dyspnea up to the fatal outcome; (*b*) from intracranial hemorrhage by the respiratory distress and signs of restlessness; and (c) from atelectasis by the lack of cyanosis and the gradual development of suppressed breathing and weakened vesicular murmur immediately after birth. The prognosis for infants with hyaline membrane disease is unfavorable; however, some recoveries have been seen.

Results of Specific Treatment of Miliary Tuberculosis in Children: A Follow-Up Study of 63 Patients Treated with Antimicrobial Agents. E. M. Lincoln and F. Hould. New England J. Med. 261:113-120 (July 16) 1959 [Boston].

In the chest clinic of the children's medical service of Bellevue Hospital, New York, 102 children with generalized miliary tuberculosis were seen between 1926 and June, 1944. Of these 102 children, 99 died within a year, 88 of them having succumbed within 3 months of diagnosis; the majority died with an associated tuberculous meningitis. The 3 patients who survived for more than a year died of tuberculosis 15 months, 2 years, and 4 years, respectively, after the initial diagnosis of miliary tuberculosis.

The unfavorable prognosis in these 102 children is contrasted with results in 63 patients treated during 12 years (between June, 1944, and June, 1956) with antimicrobial therapy. A small group of 9 children were first treated with a sulfone, thiazolsulfone; 6 of the 9 survived and remained well until 2 of them manifested renal tuberculosis and 1 pulmonary tuberculosis 11 or 12 years after the original diagnosis of miliary tuberculosis. The case fatality rate improved in the next group of 29 children treated with both thiazolsulfone and streptomycin, but meningitis developed in 6 patients under treatment for miliary tuberculosis. In the third group of 25 children treated with 3 antimicrobial agents—thiazolsulfone, streptomycin, and isoniazid—only one death occurred, and meningitis did not develop under treatment. Two children had tubercle bacilli recovered on culture from the cerebrospinal fluid, and the possible diagnoses of serous meningitis and abortive caseous meningitis are discussed.

As better antimicrobial agents were used in the treatment of miliary tuberculosis, the amount of calcification seen both in the primary complex and in the metastatic areas decreased. The rate of x-ray clearing was slowest in the patients treated with thiazolsulfone only—32 to 44 weeks. In the 2 later groups, treated with added streptomycin in one group and with added streptomycin and isoniazid in the other, this rate was an average of 13 weeks.

Diabetes Mellitus At Ages One to Five: Findings at Onset. H. S. Traisman, J. J. Boehm and A. L. Newcomb. Diabetes 8:289-293 (July-Aug.) 1959 [New York].

The diagnosis of diabetes mellitus in infants and small children is rare, and it is seldom made because of the infrequency of the disease, its sudden onset, and the fact that accompanying symptoms of anorexia and vomiting are so characteristic of many other ills of these age groups. The onset in these patients is abrupt in contrast to the gradual onset in older children and adults. The records of 110 infants and children, between 1 and 5 years of age, with diabetes mellitus were reviewed by the authors. Sixty-five children (59.1%) were male, and 45 (40.9%) were female. The interval between onset of symptoms and diagnosis ranged from 7 days to 8 weeks in 26 of 32 children, 12 to 23 months of age; from 7 days to 12 weeks in 29 of 30 children, 24 to 35 months of age; from 3 days to 12 weeks in 20 of 21 children, 36 to 47 months of age; and from 4 days to 16 weeks in 27 children, 48 months to 5 years of age. The interval between onset of symptoms and diagnosis could not be determined for 8 patients. Ninety-three children (84.5%) presented polyuria, and 89 (81%) increased thirst; the incidence of these symptoms was higher in children of the older age groups. Forty-seven children (42.7%) presented weight loss. Polyuria or polydipsia was present in 88% of the children, whereas polyuria or polydipsia or weight loss was present in 91%. Increased appetite was noted in 25% of the series, the incidence being 44.5% in the 48-month-to-5-year age group, compared with only 12.5% in the 12-to-23-month age group. Loss of appetite was found in 14.5% of the cases, with a much higher frequency noted in the youngest age group (28%).

Thirteen per cent of the children, with no striking dissimilarity among age groups, presented lethargy. Bed wetting appeared in 6% of the children, and vomiting in 4.5%. Three children were noted to be more irritable just prior to the diagnosis of diabetes, and another 3 showed a "craving for sweets." Of 3 additional children, the mothers noted that the diapers had a "sticky" feel to the touch, while 2 reported a "strong odor to the urine." Diabetes was discovered on routine analysis in 2 children and was preceded by a hypoglycemic episode in 2 others. An associated disease was found in 40 children (36%), while one-third of the entire group had an associated respiratory infection; 2 patients had an exanthematous disease, 1 had pyelitis, and 1 had vaginitis. Not a single case of a sibling with diabetes was found in this series, although a family history of diabetes was found in 28% of the cases. The authors point out that the basic principle underlying the home care and treatment of infants and small children with diabetes mellitus is thorough education of their parents.

Acute Purulent Pericarditis: Two Cases of Staphylococcic Pericarditis in Children. J. A. Martinez. Rev. españ. pediat. 15:301-323 (May-June) 1959 (In Spanish) [Saragossa].

Since the discovery and wide use of sulfonamides and antibiotics to which pneumococci are very sensitive, the main causative agents of purulent pericarditis have been the staphylococci. Purulent pericarditis is always a complication in the course of an infectious condition; it frequently remains undetected, whether it develops in an insidious or a sudden manner. The author stresses the need for a close watch and a careful, repeated examination of the patient's heart whenever there is cardiac enlargement and/or diminishment of the heart sounds.

Two cases of purulent staphylococcic pericarditis in children were observed at the pediatric clinic of the Municipal Hospital for Infectious Diseases in Barcelona. In one case the onset was sudden and accompanied by precordial pain; in the other the onset was insidious and masked by other signs and symptoms. The first patient, a 9-year-old boy, was suffering from a furunculosis of 2 months' duration, which extended over his neck and lower extremities. Eight days before hospitalization he had started coughing and had a high temperature, chills, and sweats, followed by dyspnea and pain in the left knee. Twenty-four hours after admission, he complained of precordial pain. The heart sounds were diminished, and cardiography showed heart enlargement. Electrocardiographic and hematological findings confirmed the diagnosis of staphylococcic infection with arthritis and pericarditis. Treatment consisted in the administration of several alternated antibiotics (tetracycline, erythromycin, penicillin, streptomycin, Terramycin, and Chloromycetin), plus prednisone. The blood culture became negative within 8 days, and the pericarditis was cured within a month.

The second patient, a 10-year-old boy, had a furuncle on the left forearm. One week before hospitalization there appeared high fever, chills, pain in the right hip, headache, and a disseminated urticarious exanthem. The boy became stuporous and delirious. Four days after admission, in the course of intensive antibiotic therapy and without any precordial pain, the auscultation, which was part of the careful daily examination, revealed pericardial friction and diminished heart sounds. Radioscopic examination showed an enlarged heart, and the electrocardiogram presented characteristic alterations. The diagnosis of pericarditis complicating a staphylococcic infection with osteoarthritis of the left hip was established. Treatment with several alternated antibiotics and prednisone was instituted, as in the first case. The blood culture became negative after 8 days, and the pericarditis disappeared within a month, but an ankylosis of the left hip joint remained.

DERMATOLOGY

Bowen's Disease and Its Relationship to Systemic Cancer. J. H. Graham and E. B. Helwig. A. M. A. Arch. Dermat. 80:133-159 (Aug.) 1959 [Chicago].

The authors report on 32 men and 3 women, between the ages of 38 and 87 years, with epidermoid carcinoma in situ of the skin (Bowen's disease), on whom either autopsies were performed or who were known to have died after pathological examination of surgical specimens of internal organs. Sections of lesions of the skin and internal organs, stained with hematoxylin and eosin, were studied in these 35 patients at the Armed Forces Institute of Pathology in Washington, D. C. Anatomically, the lesions were single or multiple and occurred on both exposed and unexposed areas of the body. Clinically, the lesions appeared as lenticular, polycyclic, erythematous, pigmented, crusty, scaly, keratotic, nodular, and ulcerated plaques; they were sharply demarcated from the surrounding tissue. The clinical diagnosis was most frequently some variety of carcinoma. The disease involved predominantly the older age groups, and the duration of the lesions from their onset to their surgical removal was 7.8 years. Twenty-eight of the 35 patients were observed to have one or more primary internal cancers, or a primary cancer of the skin with metastasis, at an average latent period of 8.5 years from the onset of Bowen's disease until detection of a malignant internal lesion or a metastasis from a cutaneous cancer. Twenty-six of these 28 patients had metastatic lesions or generalized spread from their primary tumors. Furthermore, 15 of the 35 patients had a total of 49 premalignant and malignant cancers of the skin that appeared on an average of 6.2 years later than their Bowen's disease. Cancer-proneness of the entire group is even more evident when it is considered that 31 (89%) of the patients had primary cancer in one or more locations. All 3 germ layers were involved, and the sites, in order of frequency, were the respiratory system, gastrointestinal tract, genitourinary organs, reticuloendothelial system, skin, breast, and endocrine system. Three of the 28 patients with internal malignant tumors also had herpes zoster during their terminal illness.

Excision of the Bowen lesion was the treatment of choice, for the process tended to recur or not to respond to x-ray therapy, desiccation, and curettage. Two lesions were apparently cured with radium. The average follow-up period for the 35 patients from the time Bowen's disease was first diagnosed until death was 3.4 years. Thus, there was a poor diagnosis once internal or metastasizing cutaneous.

cancer occurred. The short follow-up period in many of the 35 patients was due to death from internal cancer. Information was obtained from the records of 22 of the 35 patients regarding the occurrence of internal malignant tumors in their families; hereditary or some other common predisposition to the development of cancer was suggested by the occurrence of internal cancer in one or more members in the families of 8 (36%) of the 22 patients. Arsenic could not be implicated as a causative factor in Bowen's disease.

Surgical and autopsy specimens obtained from 35 patients with senile keratosis, 35 patients with squamous-cell carcinoma of the skin, and 139 patients with exfoliative dermatitis were compared with the specimens obtained from the 35 patients with Bowen's disease. In 4 of the 35 patients with Bowen's disease, the lesions invaded the corium as squamous-cell carcinoma; in 2 of the 4 there was metastasis to internal organs. Patients with Bowen's disease were statistically similar to those with senile keratosis in regard to the prevalence of associated primary internal cancer. In contrast, patients with primary cutaneous squamous-cell carcinoma had a much lower incidence of internal cancer than did those who had Bowen's disease. Primary internal cancer was much less frequent in patients with exfoliative dermatitis than in those with Bowen's disease, but the prevalence of lymphomas was about equal in the 2 groups. The association of Bowen's disease of the skin with internal and cutaneous cancer may well represent a cutaneous manifestation of a systemic carcinogenic disease process.

The Effect of ACTH and Hydrocortisone on the Human Sebaceous Gland. J. S. Strauss and A. M. Kligman. J. Invest. Dermat. 33:9-14 (July) 1959 [Baltimore].

An experimental study of the changes in human sebaceous glands after the administration of corticotropin (ACTH) and hydrocortisone was made by the authors, the subjects being 16 mentally defective inmates of the New Jersey State Colonies at Woodbine and Vineland. The subjects were divided into 3 groups: Group A comprised 6 prepuberal males; group B, 6 postpuberal females; and group C, 4 postpuberal males. In each group, half of the subjects received ACTH (Acthar gel) and the other half received hydrocortisone (Cortef). The doses of ACTH were 80 units 3 times a week in groups A and B, and 40 units daily in group C; Cortef was given in daily doses of 60 mg. to group A, 100 mg. to group B, and 80 mg. to group C. The duration of the treatment was 3 to 12 weeks in group A, 4 weeks in group B, and 6 weeks in group C. Control biopsy specimens were taken from the cheek before treatment, and from the contralateral cheek after varying intervals following administration of the drugs.

The changes in the sebaceous gland size were estimated by mere visual inspection; changes so small as to be undetectable by visual inspection would have no clinical significance. Three subjects in group A, 2 in group B, and none in group C showed glandular enlargement following administration of Acthar gel. Among those receiving Cortef, 2 in group A, 1 in group B, and none in group C showed glandular enlargement. The absence of visible changes in group C subjects is consistent with the fact that in postpuberal males the androgen-stimulated sebaceous glands have already attained maximum size and cannot develop further. In the subjects in whom enlargement of the sebaceous glands took place, the change was more consistently related to the administration of ACTH than to the administration of hydrocortisone. As the potentiality of developing acne is in proportion to the glandular size, the authors consider that ACTH has a greater acneigenic potency in comparison with the corticosteroids. It is also their opinion that induced acne is essentially the same and evolves in essentially the same way as spontaneous acne vulgaris.

Contact Dermatitis to Phenothiazine Drugs. D. Goodman and M. M. Cahn. J. Invest. Dermat. 33:27-29 (July) 1959 [Baltimore].

The occurrence of severe contact dermatitis and of other side-reactions, such as chlorpromazine hepatitis, has become rather frequent in association with the use of the so-called "tranquilizing" phenothiazine derivatives. The authors report a case of skin sensitization which developed after exposure to an experimental phenothiazine derivative, piperidylchlorophenothiazine (NP-207). The patient, a 31-year-old laboratory worker, while handling NP-207 during a pharmacological experiment, developed erythema and pruritus, which became a severe eczematous eruption covering the palmar surfaces of the fingers and the hands. The lesions improved gradually during a 10-week period of treatment and avoidance of contact with the drug. Nine months later, after a similar occurrence, the patient was patch-tested on the forearms with solutions of NP-207 and several other phenothiazine derivatives. All reactions were positive. One month later the patch tests were repeated with the same compounds plus many others in varying concentrations. After removal of the patches the test sites were exposed to 2 hours of intense sunlight. After 4 testings the patient became strongly sensitive to promethazine (Phenergan), indicating a new sensitization to this agent. Two control subjects, patch-tested under the same experimental conditions, did not develop any positive reactions.

The analysis of the skin reactions of this patient indicates that the compounds eliciting positive manifestations were those containing a chlorine atom in the 2- position of the phenothiazine nucleus. The structure of the side-chain did not seem to cause any allergic sensitization, and exposure to strong sunlight did not seem to affect the severity of the reactions. These experimental data suggest a possible structure-activity relationship which may be a factor in developing allergic skin reactions to phenothiazine derivatives and may be related to other side-manifestations that seem to have an allergic basis.

Local Injection of Vitamin A (Keramin) for Plantar Verruca. R. S. Gilbert and M. J. Williams. U. S. Armed Forces M. J. 10:843-847 (July) 1959 [Washington, D. C.].

The authors cite earlier reports on the effectiveness of vitamin A in the treatment of dermatological disorders associated with hyperkeratosis, and report on their own use of an aqueous vitamin A preparation, available as Keramin injection, in the treatment of plantar verruca in 100 patients at the U. S. Naval Training Center, San Diego, Calif. Keramin injection has a vitamin A activity of 50,000 units per milliliter. Although it has several other constituents, vitamin A seems to be the only active ingredient. The area to be treated is prepared with tincture of Merthiolate and anesthetized with 1% lidocaine (Xylocaine) hydrochloride containing 1:100,000 epinephrine. Anesthesia is usually effective with only 1 ml. A tuberculin syringe with a 26-gauge ½-in. needle is used for both anesthesia and Keramin injection. For injection of the anesthetic, the needle should be introduced at a point just outside the visible periphery of the lesion, and the solution deposited beneath the lesion. Keramin is injected deep into the verruca. The initial dosage should not exceed 0.1 ml. per square centimeter of verrucose area. Further injections are given at weekly intervals with the dosage increased weekly up to 0.3 ml. In cases of mosaic verrucae, or in an exceptionally large single plantar verruca, the lesion may be injected from several angles, at which time more than 0.3 ml. is needed. All patients remain ambulatory with only an adhesive strip for dressing. No arch supports or felt padding were used in the cases reported.

The local injection of Keramin (vitamin A) into plantar warts resulted in complete resolution in 82 and relief of pain in 95 of the 100 patients. No recurrence was observed within a 6-month period of observation. Keramin injection appeared to be equally effective in all 3 types of plantar verrucae. It is especially valuable in the multiple and mosaic varieties where other methods are inadequate. Extensive surgery with skin grafting, radiation, and the stronger caustics may now be avoided. The only side-reaction with Keramin was itching, which occurred in a small percentage of the patients.

INDUSTRIAL MEDICINE

Influenza Vaccination, Reaction Rates, and Absentee Experience. A. F. Mangelsdorff and P. H. Kriedt. A. M. A. Arch. Indust. Health 20:28-35 (July) 1959 [Chicago].

The authors cite a number of publications on the 1957-1958 pandemic of Asian influenza and report that in August, 1957, vaccination with an influenza virus vaccine containing the Asian strain was offered to the employees of the Prudential Insurance Company of America. A polyvalent vaccine, containing 500-cc. A units per milliliter of type A, A′, B, and the Asian strain viruses, was used throughout the organization, except for the Canadian office where a monovalent vaccine, containing 200-cc. A units of Asian strain virus, was used. The vaccination program was started during the first week of September, 1957. Inoculations of polyvalent influenza virus vaccine with the Asian strain were given to 16,210 employees, the subcutaneous method of administration being used. A total of 170 persons were rejected because of sensitivity to egg or egg products; 153 were rejected because of a history of severe asthmatic or hay fever reaction.

In order to calculate the effectiveness of the preventive influenza virus vaccination program, the absentee rate at Prudential was compared with that of 2 other companies of similar size and nature. One of the latter gave the influenza virus vaccine late in October; the other gave no vaccine. A diagram graphically shows the rate of absenteeism in the 3 companies in 1956 and 1957. In September, there was very little difference between the 1956 and the 1957 absentee rate. In October, however, the company giving no vaccine showed a 102% increase, while the company giving the vaccine late in October showed a 98% increase. Prudential showed only a 65% increase in absence, and in November the absentee rate was similar for both 1956 and 1957. From these figures it has been calculated that, excluding the days lost because of the reactions to the vaccination program, the Prudential employees were able to avoid 1,600 days of illness.

Occurrence of Certain Cancer Forms Among Gas-Plant Workers. A. Bruusgaard. Tidsskr. norske lægefor. 79:755-756 (June 15) 1959 (In Norwegian) [Oslo].

The tumor forms which have been in the searchlight as possibly due to occupational conditions in the gasworks industry are particularly tumors in the respiratory tract and the urinary tract. Autopsy in 125 cases of death among gas-plant workers revealed 12 cases of malignant tumors in the respiratory tract, 5 cases of cancer of the bladder, and 3 cases of cancer of the esophagus; 21 cancers were in other locations. The number of cancers in the respiratory tract was higher than was expected, as was the percentage of these cancers among the total number of cancers. The possible occupational cause of cancer in the respiratory tract is assumed to depend, in part, on the abundant smoke and dust connected with the manufacture of products containing tar and pitch, which contain cancer-producing substances. Such conditions are especially common among the so-called retort-house workers.

THERAPEUTICS

Corticosteroids in the Management of Tuberculous Lymphadenitis. J. B. L. Mathur and B. K. Khanna. J. Indian M. A. 32:403-404 (May 16) 1959 [Calcutta].

While chemotherapy has superseded most other methods previously used in the management of tuberculous lymphadenitis, it has been realized that some patients may fail to respond to chemotherapy or the response may be delayed. In such cases addition of corticosteroids has been known to hasten the resolution of the tuberculous lymph node involvement. Six patients with tuberculous lymphadenitis have been treated successfully by the administration of 5 mg. of prednisolone per day along with the usual chemotherapy. Three of these cases are reported here. The prednisolone was given along with streptomycin and isoniazid. The authors consider it significant that prednisolone proved effective in the low dosage of 5 mg. per day. They feel that corticosteroids in such low dosage act as replacement therapy and exert their beneficial effect by enhancing the host resistance. The safety of such small doses needs no comment.

Effect of a New Hormone, Triamcinolone, Combined with Specific Treatment in Tuberculosis. J. A. Pilheu and J. A. Iannello. Rev. Asoc. méd. argent. 73:125-130 (April) 1959 (In Spanish) [Buenos Aires].

The new cortisone derivative, triamcinolone (Ledercort), has a more powerful anti-inflammatory effect than prednisone; it is also free from mineralocorticoid effects (water, chloride, and sodium retention, or increased elimination of potassium). It has been used clinically with the same results as, and in smaller doses than, prednisone. The authors have used this new corticosteroid in association with specific therapy for tuberculosis in the following conditions: patients with grave tuberculosis to whom no previous treatment has been given; patients who have had previous treatment in whom there is laboratory evidence of sensitivity to isoniazid or streptomycin; and patients with advanced tuberculosis who after weeks or months of treatment show no clinical or radiologic improvement. The duration of the combined treatment has been from 4 to 6 weeks, the daily dose of triamcinolone amounting to 4 mg.

Four typical cases from the authors' experience are presented as illustrations of the technique and results of the therapeutic use of triamcinolone in pulmonary tuberculosis. These included cases of grave, untreated tuberculosis, tuberculosis associated with bronchial asthma, tuberculosis associated with malaria, and grave tuberculosis in which there was intolerance to PAS. In the first 3 cases the treatment resulted in both clinical and radiologic improvement; in the 4th case the intolerance to PAS disappeared, and the patient's general condition improved gradually. The following conditions must be present in order to warrant administration of triamcinolone to tuberculous patients: sensitivity of the tubercle bacilli to antituberculous drugs (streptomycin, PAS, isoniazid); inclusion of isoniazid in the therapy; and normal levels of glycemia.

The Results of the Treatment with Tolbutamide of 200 Diabetic Patients: A Discussion of Secondary Failure. J. M. Moss, DeW. E. De Lawter and J. J. Canary. Ann. Int. Med. 50:1407-1417 (June) 1959 [Lancaster, Pa.].

The authors report on 200 patients with diabetes mellitus, who were treated with tolbutamide in the diabetic clinic of the Georgetown University Hospital in Washington, D. C., or in the offices of the authors. Thirty-seven patients had had no previous treatment for diabetes mellitus, and 118 had previously been given from 5 to 80 units of insulin for from a few weeks to as much as 20 years. Most of the patients were instructed to follow a measured diabetic diet, but it was obvious that many of the obese patients continued to eat excessively. Most of the patients were started on 2 Gm. of tolbutamide daily, with the dose adjusted according to their response. Six obese patients were given a placebo of sodium bicarbonate before and after the administration of tolbutamide.

Good or excellent results were obtained in 98 patients (49%); 34 patients (17%) showed no demonstrable benefit from the administration of the drug; and 32 (16%) obtained a temporary beneficial effect followed by a secondary failure to respond. In 18 of these 32 patients the failure occurred after 6 months of treatment, and in 14 it occurred before completion of 6 months of tolbutamide treatment. Six of the 32 patients were aged less than 40 years. Three patients had had ketosis in the past. Six had had diabetes for more than 10 years. Eight were underweight, and 14 were grossly obese. Of the 29 who had taken insulin previously, 4 had taken more than 40 units daily. In 4 patients the failure was apparently precipitated by progression of cirrhosis, acromegaly, lupus erythematosus, and empyema. In 7 patients there was no obvious cause for the secondary failure. Because this secondary failure cannot always be predicted, it is important that patients on tolbutamide therapy be followed at intervals of from 4 to 8 weeks after initial stabilization.

The best results were obtained in the nonketotic, asymptomatic older patients with diabetes mellitus who were of near-normal weight and who took less than 40 units of insulin. Most of the primary and secondary failures were in patients who did not meet these criteria. Six obese patients obtained better results from a placebo than they did from tolbutamide. The good results often reported in obese patients are due to reduced caloric intake rather than to tolbutamide. Obese patients should be treated by diet alone, and tolbutamide used only if hyperglycemia persists. Eleven patients underwent major surgical interventions and 2 had normal pregnancies while their diabetes mellitus was controlled with tolbutamide. These conditions do not preclude the use of tolbutamide. There were no significant toxic effects from the drug.

PUBLIC HEALTH

Large-Scale Use of Sabin Type 2 Attenuated Poliovirus Vaccine in Singapore During a Type 1 Poliomyelitis Epidemic. J. H. Hale, M. Doraisingham, K. Kanagaratnam and others. Brit. M. J. 1:1541-1549 (June 20) 1959 [London].

Records on poliomyelitis in Singapore after 1946 showed that among the locally domiciled population cases occurred throughout the year. The majority of cases were seen in children under the age of 2 years, and the general picture was that of an area in which poliomyelitis was endemic, but with periodic increases in the number of cases. In August, 1958, cases of poliomyelitis due to the type 1 virus began to be reported, numbers increasing rapidly so that epidemic conditions existed. The occurrence of poliomyelitis in children over the age of 8 years was a further indication of the changing pattern of the poliomyelitis picture. It had been suggested by the World Health Organization expert committee on poliomyelitis in 1958 that in the face of an impending epidemic or where poliomyelitis of the infantile type is endemic, especially where signs are indicative of an imminent shift to the epidemic form of the disease, a trial of attenuated vaccine might be attempted. Both these conditions existed in Singapore, and the Minister of Health decided to offer, on a voluntary basis, immunization with the attenuated poliomyelitis virus vaccine. Although the epidemic was due to the type 1 virus and all reported cases were shown to be infected with this serologic type, it was decided to use a vaccine of the type 2 attenuated virus for various reasons, which are explained.

The type 2 attenuated poliomyelitis virus vaccine was obtained from Dr. Sabin, who agreed to release the vaccine on condition that adequate laboratory control could be assured. The Health Department of the Singapore Government set up a number of vaccination centers. The temperature of children attending the centers was taken, and if this was normal, they were given 0.1 ml. of a 1/10 dilution of the tissue culture fluid in a teaspoonful of sirup. A number of children were bled just before administration of the vaccine, and the type of poliomyelitis antibodies present in their serums was ascertained. The type 2 attenuated poliomyelitus virus vaccine was administered to 198,965 children, between the ages of 3 months and 10 years. Paralysis due to the type 1 poliomyelitus virus developed in only 6 of these vaccinated children. During the same period of time—that is, one week after the start of the vaccination campaign to the close of the epidemic—there were 179 paralytic type 1 cases among approximately 300,000 nonvaccinated children of the same age group.

No untoward effects followed the vaccination, and no case of paralysis due to the type 2 virus occurred in the vaccinees. Antibody response to the vaccine was highly satisfactory, although a small proportion of the children in the younger age groups failed to give detectable antibodies after vaccination. Some of the virus strains excreted by vaccinees showed slight increases in virulence to monkeys tested by intraspinal inoculation. This was not a progressive phenomenon, and strains isolated from contacts, where it could be assumed that at least one human passage had taken place, were no more virulent than those obtained direct from vaccinees. Only one case of paralytic poliomyelitis due to the type 2 virus occurred in a nonvaccinated child, and, as it was shown that wild virulent type 2 strains were circulating in a neighboring community, it was thought that this case could well have resulted from infection with such a wild strain.

Antigenic Variations Among Type 1 Polioviruses: A Study of 16 Wild-Type Strains and 5 Variants. H. A. Wenner, I. Archetti and G. R. Dubes. Am. J. Hyg. 70:66-86 (July) 1959 [Baltimore].

This study is one of several made to ascertain the extent of antigenic variation among poliomyelitis viruses. The practical importance of this research relates to the degree of antigenic homogeneity of various strains of poliovirus, and to the relationship of these to polioviruses used in inactivated or live attenuated virus vaccines. The study is concerned not only with the elucidation of intratypic antigenic structure but also with the extent to which these strains of poliovirus share heterotypic antigens. In earlier studies on type 2 strains it was found that the antigenic components entering into the constitution of these type 2 strains differed, making it possible to classify them into 3 major categories, namely, strains identical or closely related to the Lansing virus, strains distinctly different from the Lansing virus, and intermediate strains. The same methods were used in the present study with these exceptions: 1. The antigenic constitutions of the type 1 strains were analyzed with serums prepared in rabbits as well as in monkeys. 2. The method of complement fixation was used in addition to serum neutralization in the determinations of antigenic cross relationships. 3. A plaque method of measuring neutralization was developed for the present study and used for some antigenic comparisons.

Sixteen type 1 strains of poliovirus were selected on the basis of their rather wide distribution in time and place of original isolation. An antigenic analysis was made by means of the cytopathogenic roller tube, metabolic-inhibition, and complement-fixation methods. This analysis indicated that these wild-type strains share major antigens, but it also showed that these strains are very probably not antigenically homogeneous. These wild-type viruses cannot be placed in antigenic categories within type 1; rather, the pattern of "R" values obtained suggested that these polioviruses can be regarded as independent antigenic deviates. A plaque method for measuring neutralization was developed and used because it gave more reproducible "R" values than the other methods. By the plaque method 3 strains (Australia 4205, Breit, and Zellner) were clearly shown to differ from each other antigenically, thus giving support to differences observed with the other methods. Similar studies of 5 variants of the Akron strain of type 1 poliovirus provided no evidence that they are antigenically different from wild-type Akron.

Antigenic Variations Among Type 3 Polioviruses. G. R. Dubes, I. Archetti and H. A. Wenner. Am. J. Hyg. 70:91-105 (July) 1959 [Baltimore].

This report is concerned with antigenic variations among 9 type 3 poliomyelitis virus strains. Neutralization and complement-fixation tests revealed that not all type 3 viruses are identical in antigenic structure. The extent of antigenic relationship between all possible pairs of these strains ranged from 22 to 107%, with an average of 49%. This group of 9 strains was not found to be divisible into antigenic categories. For each of 2 of these 9 strains more than one kind of virus was included in the study: 5 different viruses of the Leon strain and 2 different viruses of the Mantova strain were used. These viruses were used to gain an estimate of possible antigenic variations within a strain. By using these viruses, the average intrastrain "R" value obtained was 86% (range, 56 to 122%), thus indicating that more variation was encountered among than within strains. Turbid-plaque-producing viruses of the Leon and Mantova strains were found to be paralytogenic for the monkey by the intramuscular route; these viruses were genetically labile, mutating to clear-plaque-producing viruses which had a selective advantage in monkey-kidney tissue cultures and which were of reduced virulence for the monkey.

Immediate Sensitivity Reaction to Poliomyelitis Vaccine. W. O. Thomson and D. J. B. Fletcher. Brit. M. J. 2:39-41 (July 11) 1959 [London].

The authors report on a 24-year-old nurse, who was sensitive to penicillin and, to a less extent, to streptomycin, and in whom angioneurotic, periorbital edema and mild shock occurred after the intramuscular injection of 1 cc. of poliomyelitis vaccine. Twenty-four hours later the patient had returned to normal. Because of the potential danger of contracting poliomyelitis in her work, it was decided that, despite this reaction, her immunization should be completed. Forty-one days after her initial vaccination the patient was referred to a special clinic for patients who wish to be vaccinated against poliomyelitis but who have asthma, eczema, hay fever, or allergic conditions. A course of small doses was planned, each to be given at weekly intervals, as past experience had shown that this technique was the safest with allergic persons. To this end, 0.1 cc. of poliomyelitis vaccine was given intradermally in the left forearm. Within 2 minutes a wheal developed at the site of the injection, surrounded by an area of erythema. At the same time the patient complained that her eyes were irritable. Over the next half hour the wheal on the forearm grew to a size of about 2½ by 1½ in. (6.4 by 3.8 cm.), and the erythema covered most of the forearm. Gradually her eyes became puffy, and over the next 10 to 15 minutes periorbital edema developed and increased. Restlessness, agitation, and marked trembling of the hands were noted. About half an hour after the administration of the test dose urticaria was noted on the patient's wrists, upper arms, and upper thighs. Five hours after the injection, her eyes were still slightly puffy, but most of the swelling had disappeared, as had the general erythema, the urticaria, and the wheal on the forearm.

Before poliomyelitis vaccine is administered, it is essential that the patient (and in the case of a child the parents) should be asked if there is a history of sensitivity to penicillin or streptomycin. If there is any doubt, a test dose should be given intradermally. For those who are penicillin-sensitive, a penicillin-free vaccine should be available, and penicillinase should be administered before vaccination. The chief safeguard, however, is to ensure that the medical practitioner is aware of the potential risk to patients sensitive to penicillin or streptomycin.

depression of alertness. A few, such as promethazine, are used in premedication and as a supplement during general anesthesia. Use of others should be discontinued before operation because of dangerous side-effects.

When the patient has been taking a Rauwolfia alkaloid, severe hypotension and bradycardia may occur on induction of anesthesia; therefore, therapy should be stopped three or four days before elective operations. If emergency care is necessary, 0.5 mg. of oxyphenonium and 5 mg. of methamphetamine may be given intravenously before induction. The phenothiazine derivatives such as chlorpromazine, promazine, and mepazine often cause postural hypotension and peripheral vasodilatation, which are hazardous during anesthesia. Use of these drugs should be discontinued two days before elective procedures. If hypotension occurs during anesthesia, Trendelenburg position and large doses of phenylephrine are used. Promethazine is one drug in this group with practically no disturbing toxicity or side-effects when given in therapeutic doses. It can be safely used before and during anesthesia.

Meprobamate is a hydroxypropane derivative with marked sedative and muscle-relaxing action. Rare cases of allergic reactions and nonthrombocytopenic purpura have been reported. No contraindication exists to its use immediately prior to operation. Hydroxyzine therapy may be continued until operation, and miscellaneous sedatives such as ethchlorvynol, ethinamate, glutethimide, and methyprylon are safe for use immediately prior to operation.

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Answer.—Subendocardial ischemia is characterized on the electrocardiogram by S-T segment depression. T-wave negativity, principally in the precordial leads, may or may not be present; abnormal Q waves and reduced R-wave amplitude are absent. Return to normal or preattack contour of electrocardiographic tracings may be confined to discrete microscopic foci or may involve a grossly visible layer. This gives the name subendocardial ischemia and/or subendocardial necrosis (of myocardial tissue) to the electrocardiographic alteration that may be due to such tissue change. It is usually seen in patients with coronary atherosclerosis. Since the electrocardiographic picture is not pathognomonic of this condition alone, one must not overlook the need for a complete history and clinical and laboratory data in arriving at a definitive diagnosis.

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Answer.—A sedimentation rate of the given magnitude and duration is not unusual in a patient with the clinical and physical findings presented. There is evidence of a pulmonary disease to cause an elevated sedimentation rate. The exact diagnosis may be revealed by further study. Chronic bronchitis is not likely to give a greatly increased sedimentation rate but may do so if complicated by destruction of the bronchial wall or by pulmonary involvement. A patient with virus pneumonia may be afebrile after the first few days of illness, and an increased sedimentation rate has been observed to persist for long periods. Six weeks is by no means excessive. The value of an elevated sedimentation rate would be to stimulate the search for other diseases of infectious or neoplastic nature. It must be remembered that authenticated rare instances of high sedimentation rates without an apparent organic disease have been recorded.

RADIATION AND REPRODUCTION

To the Editor:—*A 38-year-old woman had a radical mastectomy to remove an adenocarcinoma five years ago. She also received treatment with x-ray. She can remember no particular precaution to shield her pelvic organs during the treatment. She was told that she could have children if she remained free from recurrence of cancer for five years. Results of subsequent examinations and annual roentgenograms of the chest have been negative. The operative site has been free of new tumor growth. The patient became pregnant and had a normal pregnancy. She was delivered in August, 1958, of a 7-lb. (3,175-Gm.) girl; and an examination of the baby by a pediatrician revealed no congenital anomalies. Due to recent newspaper articles the patient and her husband want to know if future pregnancies would be advisable. Because of the genetic hazard of therapeutic radiation would there be an increased chance of a mutation in later generations?*

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Answer.—It is necessary to establish the amount of radiation exposure in order to consider such problems in terms of potential radiation hazard. From the information given, we do not have the needed data, but it would seem reasonable to assume that her ovaries received a total dosage of 5 to 10 rads. The radiation was received within a short period of time, but one can compare it with the figures given by geneticists for reasonable limits of accumulated dosage during procreative life. They give 10 rads as the limit for average segments of a population. Larger amounts are considered acceptable for an individual within the population and 5 to 10 rads are within the dosage range due to a 30-year accumulation from the natural background. One cannot say there is no genetic hazard associated with any specific amount of radiation, but, in light of our present knowledge, we can say it would carry only a small risk and is acceptable. The problem should not be confused with that which involves radiation during fetal development, which is a different risk for the production of congenital anomalies.

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BOOK REVIEWS

Respiratory Physiology and Its Clinical Application. By John H. Knowles, M.D., Chief of Pulmonary Disease Unit and Assistant in Medicine, Massachusetts General Hospital, Boston. Cloth. $5.25. Pp. 256, with 8 illustrations. Harvard University Press, Cambridge 38, Mass.; Oxford University Press, Amen House, Warwick Sq., London, E.C. 4, England, 1959.

For the past decade a few laboratories throughout the country have studied intensively the problems of developing laboratory methods for the study of pulmonary function. Recently a widespread interest in these methods has developed. Hospitals in every community are equipping pulmonary function laboratories. Realizing this spread in application, the author has brought together a clear description of principles, methods, and limitations of the tests developed by these several groups, with a discussion of the findings in the various states of chronic pulmonary disease. In 200 pages, with a minimum of graphs and charts, and with 400 references, the author has been able to present this work in an excellent manner. The style is simple and clear. The content is accurate, embracing all of the complexities of respiratory physiology, without requiring the reader to master them in understanding the test. The net result is a broad, clear picture of what has been accomplished in the development of pulmonary function testing.

The result from the standpoint of the clinical physician is disappointing. Ventilatory studies and a more liberal use of arterial puncture for blood gas analysis are the only tests which are productive of reliable information. Although improved spirometric techniques have produced information that correlates more accurately with the patient's clinical status, this type of information has always been available in the form of vital capacity measurements. Also, the study of arterial blood gases continues to be hampered by the inability to measure oxygen tension directly. The remaining interesting and essential tests of pulmonary function cannot as yet be recommended for routine use. This is not necessarily because of the personnel and/or equipment required, but because the tests for gas distribution, gas diffusion, perfusion-diffusion ratios, lung elasticity, and the work of breathing are not yet ready for clinical application. Nitrogen washout studies, Riley's gas equilibration techniques, and measurements of lung compliance have not yet yielded significant quantitation data useful at a clinical level.

From the standpoint of the author much has been accomplished in the development of these tests. This judgment is valid and understandable if one is content with accurate quantitation of clinical defects as an end in itself. The spread of interest in pulmonary function testing has arisen, not from the development of or accomplishments in this field but because of the recent success in the treatment of pulmonary tuberculosis and the increasing number of patients with chronic pulmonary disease. The physician confronted with these patients and supplied with a laboratory for pulmonary function testing wants to know what can be done by these methods. It is discouraging to find that he can but reassure himself as to the degree of the patient's ventilatory defect. The lack of wholehearted incorporation of these testing methods into clinical medicine may be due more to their deficiencies than to the clinician's unawareness of their benefits. Development in this field must be stimulated, not on the basis of past accomplishments but by what remains to be accomplished. The widespread general use of the pulmonary function laboratory should place an added stimulus on the backward research laboratories and demand of them a reorientation of endeavor to keep pace with the requirements of clinical medicine.

A Short Textbook of Radiotherapy for Technicians and Students. By J. Walter, M.A., B.M., M.R.C.P., and H. Miller, M.A., Ph.D., F.Inst.P. Second edition. Cloth. $10. Pp. 527, with 303 illustrations. Little, Brown & Company, 34 Beacon St., Boston 6; J. & A. Churchill, Ltd., 104 Gloucester Pl., Portman Sq., London, W. 1, England, 1959.

This is the second edition of a book originally published in 1950. As stated in the preface, it is based on a series of lectures given for student technicians. The style of writing is excellent, giving a clear and concise orientation of the material essential for an understanding of the problems of radiotherapy. While primarily intended for technicians, the book also should prove of great value to physicians undergoing training in radiotherapy as a preface to more detailed study of the subject. Of particular value is the clear and readable discussion of physics and the principles of radiotherapy, as a contrast to the more formal and often confusing approach so often encountered. The second half of this book deals with radiation techniques. This subject is covered in short and terse descriptions of techniques applicable to disease in which radiation therapy is indicated. For the technician this is adequate and for the physician therapist it is an excellent guide for further study. This book should be a valuable addition to the library of all radiologic departments for use by technicians and, in particular, by those concerned with the training of technicians and physicians who are radiation therapists.

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Studies demonstrate that these electrocardiographic changes usually accompany myocardial necrosis in subendocardial tissue, where the damage may be confined to discrete microscopic foci or may involve a grossly visible layer. This gives the name subendocardial ischemia and/or subendocardial necrosis (of myocardial tissue) to the electrocardiographic alteration that may be due to such tissue change. It is usually seen in patients with coronary atherosclerosis. Since the electrocardiographic picture is not pathognomonic of this condition alone, one must not overlook the need for a complete history and clinical and laboratory data in arriving at a definitive diagnosis.

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Robert E. Sandlin, M.D., Antioch, Calif.

Answer.—Herpetic keratitis is usually seen as an acute primary keratoconjunctivitis associated with a herpes simplex labialis or stomatitis. Antibiotics do not affect the herpes virus, but the topical use of antibiotics is indicated to prevent secondary bacterial infection. The virus can be destroyed only by the removal of the parasitized cells, either with such antiseptics as iodine or ether or by mechanical denudation.

After a primary herpetic keratitis, antibodies develop and a relative local immunity results which lasts for a period of several months, but the opposite cornea is still vulnerable to infection. Vaccination with either smallpox or influenza vaccine has failed to provide protection. The best precautions against recurrent inflammation are the avoidance of such precipitating factors as trauma, sunburn, fever, emotional anxiety, and injury to the peripheral fibers of the trigeminal nerve. The incidence of recurrence is high on the basis of individual clinical records. There are, however, no reliable figures on the percentage of recurrence in the population at large, for many cases are mild or escape diagnosis.

With recurrence, the inflammation may involve deeper layers of the cornea, producing the so-called diskiform types of keratitis with their ameboid or geographical morphology. Prior to World War II this type of recurrent inflammation was relatively benign, lasting three or four weeks and leaving only minimal scarring. In the postwar era, however, a more severe type of inflammation has been seen, persisting for many months and leading to corneal necrosis and occasional perforation. Also, many cases of a herpetic uveitis have accompanied such prolonged inflammations. It has been suggested that this represents an increase in the virulence of the virus and that in some instances it is due to the injudicious use of topically applied steroid preparations. Cortisone should not be used. When a recurrent inflammation persists, with the danger of severe complications, lamellar keratoplasty is now becoming recognized as the therapy of choice, since it removes the infected tissue, replacing it with healthy tissues, preserving some useful vision, and terminating the inflammation.

ANTICOAGULATION THERAPY

To the Editor:—*What are the indications for and the management of anticoagulation therapy in acute and chronic cerebrovascular disease?*

M.D., California.

Answer.—Anticoagulation is indicated in instances of occlusive cerebrovascular disease and cerebrovascular insufficiency in the absence of any hemorrhagic or massive intracranial lesion. All patients with the stroke syndrome should be studied by x-ray of the skull, electroencephalography, lumbar puncture, and angiography prior to the initiation of anticoagulant therapy. If any of these studies indicate a hemorrhagic or massive lesion, anticoagulation is contraindicated. Anticoagulation is contraindicated in hypertension when the blood pressure level is greater than 180 to 200 mm. Hg systolic or 110 mm. Hg diastolic. Anticoagulation therapy is used with a major vessel occlusion involving branches of the circle of Willis where demonstrated by angiography, i. e., anterior cerebral occlusion or middle cerebral occlusion. Where a partial carotid lesion is demonstrated by the angiogram and intimectomy is indicated, anticoagulation therapy is begun early and heparin may be initially used for rapid anticoagulation. This drug is given in doses of 50 mg. by deep subcutaneous injection every six hours, and the clotting time is checked by the Lee-White method twice a day. When desirable, bishydroxycoumarin therapy is begun simultaneously and heparin therapy discontinued when therapeutic levels of prothrombin activity are reached. Once the decision for anticoagulation is made, it is accomplished by the administration of 300 mg. of bishydroxycoumarin on the first day and 200 mg. on the second day; then the daily dosage is adjusted in relation to the prothrombin activity.

BLOOD SPECIMEN SELECTION

To the Editor:—*Does a fresh specimen of capillary blood give more accurate results than venous blood to which an anticoagulant has been added when examined for red blood cell count, white blood cell count, hemoglobin estimation by the Sahli method, and preparation of a blood smear for study of erythrocyte morphology and estimation of differential leukocyte count?*

Frank P. Mathews, M.D., Olympia, Wash.

Answer.—Red blood cell counts and hemoglobin estimations may be performed on either capillary or venous blood to which an anticoagulant has been added. The erythrocytes may be counted at any time after the blood is drawn, if there is no hemolysis and the sample is well shaken. The hemoglobin estimation can be performed even after hemolysis has begun. If the same techniques are always used, standards may be established and determinations can be compared. The venous blood may give somewhat higher but more uniform values, since admixture of tissue juices does not cause dilution. When capillary blood is used, it is important that the finger or ear not be squeezed and that the flow of blood be free.

Leukocyte counts can be obtained with a fair degree of accuracy from freshly drawn venous blood with an anticoagulant added. The rate of disintegration of leukocytes allows refrigerated storage for 24 to 48 hours, but this is not the best policy. No anticoagulant preserves either red or white blood cells sufficiently for reliable differentiation of nucleated cells or accurate morphologic description of red blood cells.

IDIOPATHIC TROPICAL SPRUE

To the Editor:—*Is tropical sprue idiopathic? What causes the bleeding in some patients? If hematuria occurs, what are the sources of bleeding in the urinary tract? What is the value of the banana diet? Is there any indication for the use of cortisone?* *Floyd O. Smith, M.D., Felton, Calif.*

Answer.—The disorder is considered idiopathic. Nontropical sprue in contrast appears to be associated with an abnormal response to gluten protein derived from wheat, barley, or oats. Bleeding tendencies are seen rarely in tropical sprue and are more frequent in nontropical cases. The bleeding defect is related to low prothrombin levels resulting from malabsorption of oil-soluble vitamin K. The bleeding is corrected by parenteral administration of vitamin K preparations. Bleeding after vitamin therapy in the urinary tract must be attributed to other causes. The banana diet is not of special value in tropical sprue but is helpful in nontropical sprue by eliminating wheat from the diet. Cortisone therapy improves intestinal function, but patients with nontropical sprue should follow a gluten-free diet for at least 200 days to exclude wheat protein as the agent causing malabsorption. Cortisone is of value in early period of treatment to improve absorption of foodstuffs by the small intestine, but the diet should be managed to prevent complications of corticoid therapy. Sprue secondary to lymphoma, collagen disorders, and intestinal lipodystrophy may respond only to cortisone.

ELIMINATION OF HOUSE MOLD

To the Editor:—*How can a basement be kept free of mold?*

Henry Krochmal, M.D., Meriden, Conn.

Answer.—Basements have the reputation of containing a high mold-spore level, but during humid weather the molds are not limited to the basement and often develop in any part of the house. They grow on leather, books, food, clothing, furniture, and in and on other materials. Each mold growth releases large numbers of spores which may remain suspended in the air for a long time.

Dehumidifying equipment in the basement, dry heat, and opening windows during dry weather will retard the growth of mold. Mold colonies already established will produce spores so abundantly that air decontamination is necessary. Circulation of air through filtering devices, combined with frequent and thorough cleaning of room surfaces and furnishings, is one method of spore removal.

The mycelia penetrate some materials, where they remain waiting to grow whenever conditions are favorable. There is no effective method for destroying these embedded molds except to remove the objects harboring them. Impeding the growth of molds or limiting the spore content of the air would minimize symptoms due to mold allergies. Effective measures to keep the basement free of mold are likely to be drastic ones.

FLUORIDE TABLETS

To the Editor:—*Which fluoride tablets are satisfactory and safe for the purpose of controlling dental caries? What is the dosage schedule?*

Ronald M. Thompson, M.D.
West Palm Beach, Fla.

Answer.—The council on dental therapeutics of the American Dental Association recently commented on the prescription use of dietary fluorides (*J. Am. Dent. A.* 56:589 [April] 1958). A number of forms of fluoride supplements are on the market. The only one that has been brought into conformity with the council's provisions is the product marketed under the brand name Fluoritabs. Additional products may be added to this list.

An excerpt from the council's announcement reads as follows:

> Fluoride tablets may be employed with least difficulty in localities where the drinking water is substantially devoid of fluoride. The following prescription illustrates their use:
>
> Rx: Sodium fluoride tablets 2.2 mg. Dispense 100.
> Label: Use according to written directions.
> CAUTION: Store out of reach of children.
>
> Written directions should be provided according to the age of the child as follows:
>
> (1) Before two years of age. Add one fluoride tablet to each quart of water used for drinking purposes and for the preparation of formulas and other food.
>
> (2) From two to three years of age. Every other day add one fluoride tablet to an amount of fruit juice or drinking water which the child will consume at one time.
>
> (3) After three years of age. Administer one tablet each day in an amount of fruit juice or drinking water that will be consumed at one time.

AUTOMOBILE SAFETY BELTS

To the Editor:—*I have provided my automobile with seat belts, yet I cannot induce my family to use them consistently. An alternative device is a padded shelf which pulls out from the dashboard and locks into position. What is the effectiveness of the latter as compared with seat belts?*

Sam I. Lerman, M.D., Detroit.

Answer.—This query is pertinent to the known fact that, of the number of persons who have belts in their automobiles and become involved in a crash, 80% do not have the belts fastened. This consultant has examined the padded shelf mentioned and finds it inadequate in several respects. The principal objection is that it does not provide restraint when the car is struck from the side, and the shelf, like the belt, requires a specific act or decision to bring it into place. The proper attitude in regard to the seat belt is to introduce it into one's habit pattern. In this way the belt is always in place even though one merely backs the car from the garage to the driveway. Eventually, a belt that automatically falls into place when the door is closed will offer a solution. Two of this type have been patented and appear mechanically sound.

Legislation to require motorcars to have minimum safety devices is before Congress, and letters to senators and congressmen urging the passage of H. R. 1346 and H. R. 1341 are very much needed. The two bills have been favorably reported out by the House Committee on Interstate and Foreign Commerce.

OTITIS DUE TO PSEUDOMONAS IN NEWBORN INFANTS

To the Editor:—*In the nursery for newborn infants, six or seven developed an aural discharge which caused no clinical symptoms. Cultures of the discharge showed Pseudomonas aeruginosa. Is that of any clinical significance? What is the treatment? What measures could be used in the nursery to prevent the recurrence or the spread of the infection?*

Samuel Newman, M.D., Danville, Va.

Answer.—Pseudomonas aeruginosa is a slender rod-shaped gram-negative organism that frequently causes suppuration, especially of the middle ear, in children. Destructive lesions of the skin and ulcers of the alimentary mucosa from this cause are not uncommon. It is probably involved in some cases of infantile diarrhea. In rare instances the infection may become a bacteremia with death as a possible result. Pseudomonas infections are difficult to treat because of resistance of the organisms to antibiotics. Testing of the bacilli in one laboratory revealed that 30% were resistant to all antibiotics. Control of hospital infections would require discovering by sensitivity tests whether the particular strain is sensitive to any antibiotic and, if so, its use systemically and locally. Quarantine should be established, with attention to attendants as possible carriers and to contaminated articles that are removed from the nursery.

UNDESCENDED TESTES

To the Editor:—*A 6-year-old boy has received care for several years because, by physical examination, there were no testes to be found. Endocrine therapy given at the age of 3 years failed to produce any change in this situation, and an exploratory operation has now been recommended. If there is loss of gonadal tissue would there be any testicular endocrine function? Should the exploratory operation be unilateral?*

Leonard H. Blackwell, M.D., Pontiac, Mich.

Answer.—If operation discloses testes with spermatic vessels so short that scrotal placement is impossible, the continuing retroperitoneal position will not adversely affect endocrine function. The spermatogenic epithelium will, of course, be completely destroyed. If, on the other hand, the blood supply to the testis is obstructed during the course of the difficult orchiopexy, atrophy of all the testicular elements will result. Such bilateral failure would result in eunuchism. For this reason, unilateral operation is recommended. If operation discloses a testis amenable to satisfactory scrotal placement, operation on the other side may be done after a short convalescence. If the operation on the first side reveals conditions unfavorable for orchiopexy, the contralateral operation should be canceled because it is likely that a similar anomaly exists on the opposite side.

SIGNIFICANCE OF SPUTUM CULTURE

To the Editor:—*Is Aerobacter aerogenes considered to be pathogenic when found in sputum and throat cultures?*

Dale C. Hager, M.D., Beaumont, Texas.

Answer.—The question cannot be answered unequivocally because of the interrelationships among the so-called enteric bacilli. Klebsiella pneumoniae (Friedländer's bacillus) is usually heavily encapsulated and its colonies are excessively mucoid in character. It is, for all practical purposes, indistinguishable from A. aerogenes and other related forms (Citrobacter, etc.). When the micro-organism is found in conjunction with the characteristic acute pulmonary disease it is designated Klebsiella, but in the absence of pneumonic disease it is customarily reported as Aerobacter or coliform. There is little evidence that certain strains of Aerobacter-Klebsiella can be differentiated on the basis of high virulence for man.

Coincident with, but not necessarily related to, the use of broad-spectrum antibiotics, an increase in coliform flora has been observed in the upper respiratory tract. When hemolytic coliform bacilli occur in heavily pure culture, they may be associated with the inflammatory reaction of sore throat, but a causal relation is not thereby established.

KLEPTOMANIA

To the Editor:—*A girl now aged 15 has been stealing objects of small value since the age of 6. Rings seem to fascinate her the most. This is evidently a case of kleptomania. Would psychiatric care help this child? Would this trait be inherited by her children?*

A. C. Scott, M.D., Evansville, Ill.

Answer.—This patient ought to receive psychiatric care and should be helped by treatment. Children who feel basically deprived in essential personal relationships sometimes give expression to their feelings by stealing. The child who feels unloved or discriminated against by the parents does the stealing as an unconscious attempt at symbolic gratification for the need not met in actual life. An essential part of treatment is helping the parents understand the nature of the difficulty so that they may help the child by more adequately meeting his need for affection and understanding. Neurotic symptoms are not transmitted to children on a hereditary basis. Any neurotic attitude, if not modified by treatment or by healthy normal maturation, can unfavorably influence the manner in which the parent cares for and rears children. The child could then betray a neurotic pattern that may or may not be similar to that of the parent.

USE OF PARALDEHYDE

To the Editor:—*The following questions relate to the use of paraldehyde in the treatment of a chronic alcoholic who is otherwise in good health, except for mitral valve damage from rheumatic fever. What is the length of therapy and the dosage that can be safely given? Can it cause tissue damage? What would be a substitute medicament?* *M.D., Nebraska.*

Answer.—The effects of paraldehyde are similar to those of alcohol, and when addiction develops the manifestations are also similar and include the possibility of delirium tremens during withdrawal. Toxic effects result from paraldehyde that has decomposed due to exposure to light or other reasons to form acetaldehyde. A report of renal tubular acidosis resulting from paraldehyde ingestion was given by Elkinton and others (*Am. J. Med.* 23:977 [Dec.] 1957). During six years of follow-up the patient ingested 60 to 120 cc. of paraldehyde a day. There are reports of organ damage from paraldehyde. The rheumatic heart disease with mitral stenosis would not be affected by the paraldehyde. There is no less toxic drug which could be substituted.

URINARY BLADDER CAPACITY

To the Editor:—*An elderly woman was hospitalized for suppurative meningitis. On the 10th day she developed azotemia and a gradually enlarging mass in the lower abdomen. She was voiding 1,200 to 1,400 cc. of urine a day, but because of the azotemia and the mass, which had now extended above the umbilicus, she was catheterized. The mass disappeared as 4,800 cc. of urine was drained out, and the azotemia improved. Since this procedure she has not been able to void voluntarily. She has been on therapy with bethanechol chloride. How much urine can the bladder contain? How thin will the bladder wall be when distended to the capacity of 4,800 cc.?* *A. D. Talusan, M.D., Baltimore.*

Answer.—Textbooks indicate a maximum bladder capacity of 2,000 to 4,000 cc. The greatest recorded volumes retained by the urinary bladder are 9,000 cc. in one patient and 11,000 cc. in another. The thickness of the bladder wall may vary from 1 to 10 mm., and one can only guess that it would be less than 1 mm. when containing 11 liters of urine.

SYMPTOMS OF CORONARY DISEASE

To the Editor:—*A patient had a coronary occlusion one year ago and since has been taking 200 mg. of phenindione daily, 0.25 mg. of digoxin daily, and a tranquilizer. For several months there has been a tingling, sensations of pricking, formication, and a feeling of coldness or anesthesia in the right upper extremity and right side of the face. Could these symptoms be due to drug sensitization, or are they part of the thrombosis? Could concurrent arthritis cause the sensations?*
William J. MacDonald, M.D., Boston.

Answer.—Drug sensitization does not produce the symptoms described. Such symptoms in the upper extremities are frequent after a coronary thrombosis, and they less frequently are felt in the face. Spondylitis, arthritis of the shoulder joint, and other skeletal lesions may be sites of referred sensations due to arteriosclerotic heart disease. For example, a patient with an old ununited fracture of the left humerus had pain which was relieved by nitroglycerin and was felt only at the site of his old fracture. When he later had a myocardial infarction, the pain was again at the site of the old fracture.

CARCINOMA IN SITU

To the Editor:—*A 43-year-old patient had a panhysterectomy for epidermoid carcinoma in situ of the cervix. Should estrogen be given if the patient needs control of menopausal symptoms?*
William E. Ehling, M.D., Streator, Ill.

Answer.—There would be no contraindication to the administration of exogenous estrogens in a patient who has had proved carcinoma in situ of the uterine cervix. This would be based on the fact that total hysterectomy with preservation of the ovaries is an accepted form of treatment for this condition.

YELLOW SKIN IN INFANTS

To the Editor:—*A 10½-month-old child has had yellow discoloration of nasal labial folds and both ears. The rest of the body, including the scleras, shows no discoloration. There has been no excessive vitamin ingestion, and the color varies in intensity but never quite disappears. The child is developing well. Please explain this phenomenon.*
George Vash, M.D., Lonaconing, Md.

Answer.—It is not possible to give a satisfactory answer to this question without more information. If the pigmentation is really yellow and jaundice and drugs (quinacrine hydrochloride and picric acid) are not implicated, it is possible that this pigmentation is due to carotenemia or xanthomatosis. The localization of the discoloration to the nasal labial folds and ears is compatible with carotenemia. Carotenemia can be diagnosed by determination of the level of serum carotene. Carotenemia is common in infants. A person with xanthomatosis has either localized nodules or diffuse yellowing of the entire skin surface. Other possible causes would be myxedema and diabetes mellitus.

VITAMINS B_6 AND B_{12}

To the Editor:—*Is there any advantage for people of the middle-age group to partake daily of vitamins B_6 and B_{12} if there is no medical indication for them? Will a daily intake of them at the average dosage of 10 mg. do any harm?*

Jacob M. Cahan, M.D., Philadelphia.

Answer.—Vitamins, like other medicaments, should not be administered without definite indication. There is no definite advantage for middle-aged people to take vitamins B_6 and B_{12} in quantities of 10 mg. daily. The human requirement for neither of these vitamins is firmly established, but evidence would indicate that the dietary requirement of vitamin B_6 is much less than 10 mg. per day and that there is little likelihood that an ordinary diet in the United States would be deficient in this factor. The daily requirement for vitamin B_{12} is a few micrograms or less per day. An amount of 10 mg. per day would exceed any possible human requirement. There is no evidence to indicate that excessive quantities of vitamins B_6 or B_{12} would be harmful. The cost of such quantities is not inconsequential however.

JUTE FIBER PNEUMOCONIOSIS

To the Editor:—*Is pneumoconiosis caused by the inhalation of jute? A carpet layer, who is 38 years old, has increasingly severe dyspnea, and he has a chest expansion of only 1 in. Jute is a common component of carpet padding.*

Seymour A. Hartman, M.D.
Sherman Oaks, Calif.

Answer.—Contact with jute has been identified with dermatitis due to the oils and soaps used in the primary preparation of the jute. Jute itself may be an irritant or allergen causing dermatitis. A variety of pulmonary tract involvements from jute, including laryngitis, bronchitis, asthma, pneumonitis, emphysema, and bronchopneumonia, are referred to as "mill fever," which is a transient, three-to-four-day illness believed to be related to an allergic response to the vegetable fiber. It is not known that such conditions appear in persons with trades such as carpet laying, in which the exposure may be minimal.

MINERAL SPIRITS AND RESPIRATORY IRRITATION

To the Editor:—*A patient developed the sensation of tightness of the throat which occurs occasionally, accompanied by a dry cough and some dyspnea. These symptoms last for a week, disappear, and then recur. He is a 44-year-old man who works in an automobile factory where part of the work is to wash metal parts in a solution of mineral spirits. Is there a possible relationship between this work and his respiratory difficulty?*

B. Goldberg, M.D., Chicago.

Answer.—Mineral spirits is a petroleum fraction akin to naphtha and kerosene. In low concentration its vapors may produce irritation of the eyes and respiratory tract. In comparison to other petroleum liquids it has a relatively high boiling point and evaporates slowly. Thousands of workers are exposed to this chemical each day without medical sequence. It is unlikely that any significant dyspnea could be traced to this cause.

DISASSOCIATION OF TWINS

To the Editor:—*Are there psychological or medical reasons for advising the parents of twins to separate the children in their classrooms on starting school?* *M.D., Illinois.*

Answer.—It is desirable to gradually bring about some separation between twins. When together constantly and dealt with as though they were one, the children tend to rely exclusively on each other and may not reach out toward association with other children. It is easier for each to attain a sense of identity if they are not together constantly. If they differ in abilities there will be less competitiveness when they are separated. Separate classrooms when feasible are preferred. In the same classroom, however, a teacher can bring about a degree of separation and should make an effort to handle them as individual children.

SODA LIME REFILL SCHEDULE

To the Editor:—*How often should the soda lime be changed or replenished in the canister of a closed-circuit anesthetic machine? The machine is used with nitrous oxide and oxygen for obstetric deliveries.*

Homer G. Ellis, M.D., Centreville, Miss.

Answer.—In anesthesia machines with a single small soda lime canister, the material should be changed after four to five hours of use. In machines with larger canisters, which usually contain 1,300 to 1,400 Gm. of soda lime, the material should be changed after 10 to 11 hours. Many carbon dioxide-absorbing materials contain an indicator which causes the absorbent to change color when it becomes exhausted. This change of color is a gross test and not infallible but is helpful in detecting exhausted soda lime.

ELASTIC BANDAGE APPLICATION

To the Editor:—*Have standards been set for the use of elastic bandages with regard to method of application and amount of pressure to be applied? What is the use of molded shoes in the treatment of disorders of the foot and leg?*

Fred Stern, M.D., Brooklyn, N. Y.

Answer.—There is no standard technique for the method of application or for the amount of pressure to be applied with an elastic bandage. This varies with the condition for which it is used. The technique is to have the bandage overlap itself about half its width. The amount of pressure should never exceed the amount of elasticity of the bandage. The technique of molded shoes for the most part has been in the hands of custom shoe builders.

HEPATITIS AND DIET

To the Editor:—*Is chocolate harmful for people who have had hepatitis or other liver disease? How long after virus hepatitis should one refrain from alcohol?*

Francis Willner Epstein, M.D., Toledo, Ohio.

Answer.—Diets prescribed for patients who have hepatitis or diseases of the liver should be low in fats. Chocolate contains 30 to 50% cocoa butter and is a concentrated source of fat. Alcohol is rapidly absorbed from the fasting stomach and goes to the liver, where excessive amounts would cause damage. A patient with hepatitis should be deprived of alcohol until the serum bilirubin level is normal and the cephalin flocculation value has returned to 1+. The time is usually two years.

COLORED BASEBALLS

To the Editor:—*Is a colored baseball (yellow or orange) more visible and more safe than a white one? The colored ball size would be about 2.9 in. in diameter. Baseball is played in the afternoon and early evening until dusk.*

Robert E. Murto, M.D., Trenton, N. J.

Answer.—A white baseball has a higher reflectivity of luminance than one of any other color. Visibility is lessened by smudge, so a plastic finish that allows dirt to be easily wiped off would be advantageous. When a ball is used in twilight, increased visibility would result if six dime-sized spots in blue-green phosphorescent paint were placed equidistantly on it.

HOMOLOGOUS KIDNEY TRANSPLANT

To the Editor:—*Has there been, recently, a successful kidney homotransplant in a human being other than an identical twin?*

John Bartness, M.D., Albert Lea, Minn.

Answer.—One transplant has been done between twins who were not identical. This was successful for more than three months. Bilateral nephrectomy was performed on the recipient on Feb. 4, 1959, and his state of health is still excellent. Dr. John P. Merrill directed the medical care, Dr. James B. Dealy administered total body radiation of 250 r and 150 r, and the operation was performed by Dr. Joseph S. Murray and Dr. J. Hartwell Harrison.

NASAL ULCER

To the Editor:—*A 35-year-old man has an ulcer in the nasal vestibular mucosa over the lateral cartilage. There is an amber-colored granular crust, which wipes off easily. There is no bleeding. Tests show a few polymorphocytes in smear of the nasal discharge and hemolytic staphylococcus by bacterial culture. What is cause and treatment?* *M.D., Michigan.*

Answer.—In view of the laboratory findings, one would use an antibiotic or sulfonamide systemically and topically to treat the hemolytic staphylococcus infection.

SLEEPING POSTURE

To the Editor:—*Would any deformity develop as a result of sleeping with a small pillow between one's knees?* *M.D., Tennessee.*

Answer.—There is no apparent deformity that would occur in an adult with normal extremities from this use of a pillow. The patient with arthritis, using a pillow under the knees, could develop a flexion contracture. In children no deformity would occur, and it is possible that a pillow between the knees, as a splint with the ankles held together by bandaging, might be of some value in correcting knock-knees.

TRANSFUSION REACTION AND SEX FACTOR

To the Editor:—*Is it possible that the presence or absence of chromatin sex factors is important in blood transfusion reactions of undetermined cause, i. e., male recipient of blood from female donor and female recipient from a male donor?*

Herman Goodman, M.D., New York.

Answer.—There are no reported complications which are attributed to the use of blood for transfusion when the donor is of the opposite sex and all other factors are compatible. It is possible, however, that future work may show some sequela due to transfusions of this type.